SOLUTION OF SELECTED POPULATION BALANCE EQUATIONS BY THE METHOD OF WEIGHTED RESIDUALS

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It is certified that this work has been carried out under my supervision and that this has not been submitted elsewhere for a degree.

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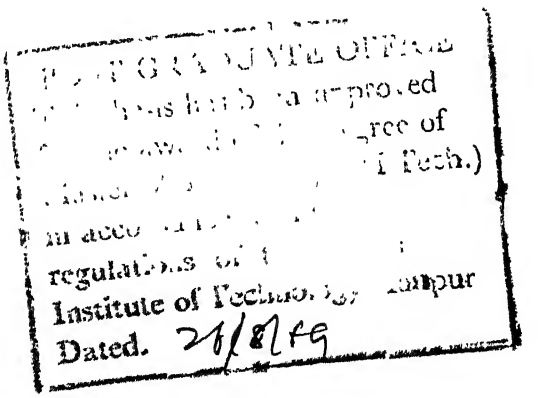

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ABSTRACT

Integro-partial differential equations from a population balance model for a continuous microbial propagator in which rod-shaped organisms grow have been solved using the method of weighted residuals. Since the domain of interest is semi-infinite, a linear combination of Laguerre polynomials, which are complete in the space $(0, \infty)$ has been assumed as the trial solution. The orthogonality property of these polynomials has been used to advantage in securing an exact moment condition for the population distribution.

The trial solution is substituted in the pertinent differential equation and the unknown parameters in the assumed solution determined by orthogonalization of the equation residual with members of a family of functions complete in the space $(0, \infty)$. Both the steady state and unsteady state solutions have been obtained using three different weighting functions and the results are in good agreement. It is found that the final solution is approached in both the cases with about eleven functions. The solution to the steady state equation has been checked by two successive approximations. The batch propagator has been

CHAPTER - I

INTRODUCTION

Population balance equations represent a number balance of particles on particulate systems in which the number of particles is continually subject to change by the disappearance of existing particles or appearance of new particles or both. In chemical engineering, they form a sound basis for the theoretical understanding of continuous crystallization, grinding, microbial propagation, multi-phase suspensions and catalytic fluidized reactors- subjects hitherto handled with a good amount of empiricism.

In all the above systems, each particle may be characterized by a specific set of properties, for example the size of the droplets in a dispersed phase reactor or of crystals in a continuous crystallizer or the physiological state of the micro-organisms in a microbial culture. For a mathematical characterization of such systems, a population balance equation is found necessary.

Whenever a system containing a large number of particles has to be studied, as in the Kinetic Theory of Gases, the overwhelming complexity of detail necessary to describe the state of the system and its interaction with the environment forces one to adopt a probabilistic or

like the Boltzmann equation, are usually partial differential and often in tegro-differential equations. The equations contain "Source" terms which account for the appearance of new particles and "Sink" terms which arise due to disappearance of existing particles. These "Source" and "Sink" terms depend on the system being described.

1.1 The Need for Population Balance Equations:

The applications of the principles of conservation of mass, energy and momentum in engineering contexts to homogeneous systems is familiar to the chemical engineer. In these cases the equations of change furnish an adequate mathematical characterization of the system being studied. However there are many problems of engineering importance involving heterogeneous systems like two phase suspensions which cannot be handled within the framework of the conventional conservation equations alone; the proper formulation of the equations of change demands a population balance. For these systems, the distribution of entities about spatial (or more likely property) coordinate axes is of dominant importance. For example continuous crystallizer design is based to a large extent on the size distribution of crystals in the vessel and catalytic fluidized reactor design on the activity and area distribution

give a better understanding of many selectional mechanism in growth.

The general nature of population balance equations for systems in which an individual particle is characterized by a vector quantity has been given by various authors(2,3,9).

Hulburt and Katz(2) have formulated a class of problems in particle technology in terms of equations similar to those of classical statistical mechanics and shown how these equations can be tied in with the differential material and energy balances commonly used to describe the performance of pieces of chemical equipment. The main problems t reated are those of particle nucleation, growth and agglomeration. The assumption of simple forms of expression for growth and nucleation and absence of breakage or fission phenomena enabled the authors to simplify the original partial differential equations to ordinary differential equ ations in the moments of the distribution. Once the moments were known, the distribution could be fitted using the appropriate orthogonal polynomials of the given space. The general equation given by them for a particulate system in which the individual particle is characterized by a vector x is

$$\frac{\partial W_x}{\partial t}(\vec{x},\ t) + \nabla_{\vec{x}} \cdot \dot{\vec{x}}\, W_x\ (\vec{x}\ ,\ t) = h(\vec{x},\ t)$$

W_x = Non-Normalized distribution of particles in state between $\bar{x}$ and $\bar{x} + d\bar{x}$

$\dot{\bar{x}}$ = growth rate of particles

∇ is the gradient in $\bar{x}$ space

$h(\bar{x}, t)$ is the net rate of appearance of particles in state $\bar{x}$

A.D.Randolph (3) has derived a general form of a population continuity equation. He has further transformed it into a more useful form applicable to the majority of engineering problems and focussed attention on the similarities with respect to the more common engineering conservation equations.

1.2 Chemical Engineering Applications:

Randolph and Larson (4) have applied the idea of conservation of population for the analytical study of crystal size distribution in a continuous crystallizer. Equations relating population density to size, both in the steady and transient states have been presented and solved. Assumptions were made to simplify mathematically intractable cases. Crystal size distributions have been obtained for several modes of crystallizer operation - Arbitrary solids concentration, seed crystal removal, product classification, and staged vessels. The effect of holding time and feed supersaturation on crystal size has been investigated.

Pehnken,Horowitz and Katz (5) have given a mathematical formulation for determining particle size distributions in mixing vessels where each particle, while in a vessel grows or shrinks according to a prescribed differential law. The application studied is a catalytic fluidized reaction system where the catalyst particles are recycled between two zones, one in which they are loaded with reagent, and one in which they are stripped of product. Steady state size distributions have been developed along with expressions for average loading and stripping rates. Procedures are given for following transients.

Fredrickson, Tsuchiya and Co-workers(6,7,8) have introduced the idea of conservation of population with respect to age and size distributions in microbial cultures. Fredrickson et.al have also provided more general equations for microbial population by attributing a "vector state" to characterize an individual cell (9). In this"vector state description" of the microbial cell, the physiological state of the cell is specified by its biochemical composition, assuming that the intra-cellular structure is of a relatively simple nature. Growth and fission are described by a Markov process, that is these depend only on the cell's current physiological state and not on how that state had been

derived, as well as an equation of change for the state of the cellular environment. These equations allow us to predict the statistical and dynamical behaviour of a cell population from information obtained by analysis of cellular and sub-cellular structure and function.

1.3 Solution of Population Balance Equations:

Gaudin and Meloy(11) have derived a comminution distribution equation considering both single and repeated fracture. The resulting integro-differential equation has been solved using a finite difference approximation.

K.J. Reid (12) has presented a practical approximation and developed a solution for the fundamental integro-differential equation for batch grinding. The solution has been written in terms of two experimentally determined parameters of the system - rates of breakage and a breakage function.

Valentas and Amundson (13) have developed a mathematical model which relates the breakage of droplets in a two-phase system to the distribution of droplet sizes. The conservation equation leads to a Volterra Integral equation in the steady state. This involves the influent distribution function, the vessel distribution function and a Kernel describing the breakage mechanism. This has

feed distribution, perfect mixing and binary breakage with formation of equal sized daughter droplets. A numerical solution has been developed for the more complicated case where a normal distribution about the mean of the sizes of the daughter droplets formed from breakage of larger droplets is assumed. The integral term is approximated by an integration formula and the solution of the equation obtained by collocation Method. Solutions have been also obtained for the case where the breakage frequency depends on size and for limited breakage where droplets below a certain size are stable and do not break. In another paper (14) where coalescence is also considered, an expression for the coalescence frequency distribution has been developed by an analogy to collision in a second order reaction. The steady state equations have been solved numerically with an iterative procedure for the final system of nonlinear equations. The transient equations for a stirred-tank vessel and a batch vessel have been solved by approximating the breakage and coalescence integrals by integration formulae and solving the resulting system of differential equations by a predictor-corrector method.

Ramkrishna (10) et.al have solved the population

of successive approximations on a computer.

Bakman (7) has solved the population balance for a continuous microbial propagator based on a mass model for the case where the cells divide into two identical daughter cells. Solutions were obtained by a predictor-corrector method for spherical and rod-shaped cells. Exponential batch propagation is considered on similar lines.

1.4 Scope of the Present Work:

Population balance equations become integro-differential or integral equations when "new" particles are formed from existing particles or due to interaction between existing particles. Additional complication is introduced when there is growth, as in a biological culture with which the present work is concerned. Growth terms can arise when any property associated with the individual particle changes with time. Thus in dispersed phase systems if one chooses to describe the mean concentration of a transfer species as a property of the individual droplet, then this would change with time as a result of mass transfer.

Experiments may dictate a maximum size of particle

organisms for example, the form of the growth rate expression does not permit one to fix a maximum size of cell. Hence an infinite domain may arise.

Solutions to population balance equations of the above type are non-existent in the engineering literature.

It is intended to solve the population balance equation for a continuous microbial propagator in which rod-shaped organisms grow by a classical approximation scheme, the method of weighted residuals.

CHAPTER - II

POPULATION BALANCE EQUATIONS FOR A MICROBIAL PROPAGATOR

The system with which the present work will be concerned is a perfectly mixed vessel containing microbial cells and substrates. A feed stream containing fresh substrate but no cells is introduced into the vessel, while an effluent stream of the same volumetric flow rate removes the cells, substrates and products from the vessel. A constant culture volume is thus maintained within the vessel. This system will in future be referred to as a "continuous microbial propagator".

The cells in the propagator grow by consuming substrates from the environment and multiply in number by a random binary fission process. Growth and increase of population bring about changes in the cellular environment both by uptake and release of chemical products by the cells. The nature of the cellular environment in turn affects the rate of growth and multiplication of the population. The mathematical model adopted for the description of the behaviour of the microbial population in the propagator will be the one developed by Eakman(7,8).

The model is segregated in the sense that cells are distinguished as individuals. Further, it is structured, so that differences between cells are recognized. The interaction of the population with the environment will be explicitly taken into account. Eakman (7) considered both cell mass and cell age and concluded that cell mass is a better index of the state of the cell. Hence the mass model will be used throughout.

2.1 The Population Balance Equation for a Continuous Microbial Propagator:

Define

$W(m, t)\, dm$ = the number of cells per unit volume (population density) with mass between m and m + dm

$\Gamma(m, C_{sk})dt$ = the probability a cell of mass m at time t will divide in time t to t + dt.

$p(m, m')dm$ = the probability a daughter cell formed from a mother cell of mass m' has mass between m and m + dm.

$H'(m, C_{sk})dt$ = the probability a cell of mass m at time t will die in time t to t + dt.

$r(m, C_{sk})$ = the rate of mass increase (growth rate) of a cell of mass m in environment with nutrient concentration(s) C_{sk}

The partial integro differential equation describing the distribution of masses at any time is obtained by making a number balance on cells of a given mass, similar to the technique one adopts in deriving the conventional equations of change, or that given by Randolph (3). This gives

$$\frac{\partial W(m, t)}{\partial t} + \frac{\partial}{\partial m}\left[r(m, C_{sk})\, W(m, t)\right] = 2\int_{m}^{\infty} \Gamma(m', C_{sk})\, p(m, m')\, W(m', t)\, dm' - \left[\frac{1}{\theta} + \Gamma(m, C_{sk}) + H'(m, C_{sk})\right] W(m, t) \qquad \ldots(2.1)$$

The first term on the left hand side represents the accumulation term. The second term is that due to growth in and out of the given mass range. The first term on the right hand side refers to the number of cells formed by binary fission of larger cells to produce daughter cells in the given mass range. The second term includes the loss in number by washout, fission and death respectively; θ is the holding time, the transition probability for washout in a perfectly mixed vessel being $\Delta t/\theta$.

Boundary conditions on the solution are obtained by considering an independent balance on population density in the propagator

$$\frac{dN}{dt} = \int_{m}^{\infty} \Gamma(m', C_{sk})\, p(m, m')\, W(m', t)\, dm' - \left[\frac{1}{\theta} + \Gamma(m, C_{sk}) + H'(m, C_{sk})\right] N$$

The number density N(t) is related to the distribution W(m, t) as its zeroth moment. Thus

$$N(t) = \int_0^\infty W(m, t)\, dm \qquad \ldots(2.3)$$

Integrating equation (2.1) over all m and comparing the resulting equation with (2.2) one obtains

$$r(\infty, C_{sk})\, W(\infty, t) = 0 \qquad \ldots(2.4)$$

which is the regularity condition stated by Behnken et.al.(5).

Since the behaviour of a cell depends upon the substrate concentration in the environment, a substrate balance is made on the propagator. For an arbitrary ith substrate a mass balance gives

$$\frac{dC_{si}}{dt} = \frac{1}{\Theta}(C^\circ_{si} - C_{si}) - \int_0^\infty \beta_i(m)\, r'(m, C_{sk})\, W(m, t)\, dm + \int_0^\infty \gamma_i(m)\, r''(m)\, W(m, t)\, dm \qquad \ldots(2.5)$$

Where C°_{si} is the concentration of the ith substrate in the feed stream; β_i represents fraction of ith substrate in the total amount of mass taken up the cell; $r'(m, C_{sk})$ is the rate of mass uptake of a cell. The net rate of mass increase for the cell $r(m, C_{sk})$ is the difference between the rate of mass uptake $r'(m, C_{sk})$ and the rate of mass release by the cell r"(m)

γ_i is the fraction of ith product in the total mass released by the cell.

Equations (2.1) and (2.5) subject to the boundary condition (2.4) and appropriate initial conditions thus form the mathematical problem which is to be solved.

2.2 Growth of a Single Rod-Shaped Cell:

Von Bertalanffy (15,16) reasoned that since all mass added to a cell must cross the cell surface, the rate of uptake should be proportional to the surface area of the cell. Further the rate of release should be proportional to cell mass since materials released are presumably products of catabolic reactions. It was assumed that the rates of these reactions were proportional to cell mass. Thus

$$\frac{dm}{d\tau} = r(m, C_{sk}) = \phi S - \mu_c m \qquad \ldots(2.6)$$

By knowing how the cell geometry changes with growth for a rod shaped cell, an expression may be written for the growth rate(7).

$$\frac{dm}{d\tau} = \left(\frac{2\phi}{R\rho} - \mu_c\right)m + \frac{4}{3}\pi R^2 \phi \qquad \ldots(2.7)$$

ρ is the volume average density of a single cell and R the cylindrical radius. It is assumed that the flux term ϕ is of Michaelis-Menten form

$$\phi(C_s) = \frac{\mu' C_s}{\ldots} \qquad \ldots(2.8)$$

where C_s is the concentration of the limiting substrate in the environment. It is assumed henceforth that there is a single limiting substrate. The second term in (2.7) is the contribution of the spherical end caps of the cylindrical cell and may be usually neglected.

Integration of (2.7) for constant environment provides, after neglecting the end cap contribution,

$$m = m_o \, e^{\left(\frac{2\phi}{R\rho} - \mu_c\right)\tau} \qquad \ldots(2.9)$$

Equation (2.9) shows that rod-shaped cells increase in size in an exponential manner with cell age and can in a mathematical sense reach arbitrarily large sizes. Thus the domain of interest should be $(0, \infty)$ for rod-shaped cells. This is not so for spherical cells (7) where there is a limit to the maximum size attainable.

2.3 Single Cell Division:

Schaechter et.al(17) have found that the size of a cell at division has a smaller coefficient of variation than cell age at division which indicates that cell size and hence cell mass is a better predictor of cell division than cell age. Cell division being a random process, it is found that the masses of cells at division are found to be distributed around a mean. A less realistic assumption would be that

assumed in this work to be of a Gaussian type

$$h'(m) = \frac{2e^{-\frac{(m - m_c)^2}{\epsilon}}}{\epsilon\sqrt{\pi}\left[1 + \mathrm{erf}\left(\frac{m_c}{\epsilon}\right)\right]} \qquad \ldots(2.10)$$

By Bayes theorem of probability, one can relate the probability that a cell of mass m will divide in time t to t + dt, $\Gamma(m, C_s)$, to the probability that a dividing cell has mass m, h'(m).

$$\Gamma(m, C_{sk})\, dt = \frac{2\, e^{\left(\frac{m - mc}{\epsilon}\right)^2} \gamma(m, C_{sk})}{\mathrm{erfc}\left(\frac{m - mc}{\epsilon}\right)} dt \qquad \ldots(2.11)$$

using $dm = r(m, C_{sk})\, dt$

ϵ is the standard deviation of the distribution. Since $r(m, C_{sk})$ depends on cell geometry and time, $\Gamma(m, C_{sk})$ will also depend in general on geometry and time.

In the cell division process, a large number of replicated entities like nucleic acids are allotted to each daughter cell. If this allocation is random, then the mass of the newly formed cell will be random. In the present work the distribution of the cell masses at division will be chosen arbitrarily. One can choose any distribution satisfying the symmetry condition $p(m, m') = p(m' - m, m')$ and the normalization condition

$$\int_{0}^{m'} p(m, m')\, dm = 1 \qquad \ldots(2.13)$$

since a cell at division cannot have a mass more than the parent cell. It is assumed that the distribution of the daughter cell masses does not depend on the cellular environment. The distribution of daughter cell masses that will be used here is

$$p(m, m') = \frac{30\ m^2\ (m' - m)^2}{m'^5} \qquad \ldots(2.14)$$

which satisfies (2.12) and (2.13)

2.4 The Biomass Balance for a Continuous Propagator:

On neglecting the spherical end cap contribution to the growth of rod-like cells, equation (2.7) can be written as

$$\frac{dm}{d\tau} = \left[\frac{2\ \phi(c_s)}{R\rho} - \mu_c\right] m \qquad \ldots(2.15)$$

The first moment of (2.1) is

$$\frac{dC}{dt} = \int_0^\infty r(m, C_{sk})\ W(m, t)\,dm - \frac{C}{\theta} - \int_0^\infty m\ \textcircled{H}'(m, C_{sk})\ W(m, t)\ dm \qquad \ldots(2.16)$$

where the first moment

$$\mu_1(t) = \int_0^\infty m\ W(m, t)\ dm \qquad \ldots(2.17)$$

is the biomass concentration. Substitution of (2.15) into (2.16) and (2.5) and integration gives for the rate of change

$$\frac{dC}{dt} = -\frac{C}{\theta} + \left[\left(\frac{2}{R\rho}\right)\frac{\mu' C_s}{K_s + C_s} - \mu_c\right] C \quad \ldots(2.18)$$

and for rate of change of substrate concentration

$$\frac{dC_s}{dt} = \frac{1}{\theta}(C_s^\circ - C_s) - \frac{\beta.2}{R\rho}\frac{\mu' C_s C}{(K_s + C_s)} + \gamma\mu_c C \quad \ldots(2.19)$$

Equation (2.18) is a condition for the first moment of W(m, t) that can be determined once the cell parameters are known by simultaneous solution of (2.18) and (2.19). It must be noted that the form of (2.19) leads to biomass and substrate balances (2.18) and (2.19) which do not involve W(m, t). This is not true in general where (2.15) could have a more complicated form as for spherical cells where biomass and substrate concentration cannot be obtained without first solving for the cell mass distribution. Alternately if the kinetics of growth is known in terms of distributed model parameters like biomass and substrate concentrations then it is possible to have the first moment and substrate balance equations uncoupled from the population balance equation.

Equation (2.15) can thus be cast in a form $r(m, C_s) = f(t)m$ where $f(t)$ contains substrate concentration terms which are determined from equations (2.18) and (2.19). Equation 2.1 becomes

$$\frac{\partial W(m,\ t)}{\partial t} + \frac{\partial}{\partial m}\left[m\ f(t)\ W(m,t)\right]$$

$$= 2\int_{m}^{\infty} \Gamma(m',\ C_s)\ p(m,\ m')\ W(m',\ t')\ dm'$$

$$-\left[\frac{1}{\theta} + \Gamma(m,\ C_s) + \textcircled{H}'(m, C_s)\right] W(m,\ t) \qquad \ldots(2.20)$$

Equation (2.24) has to be solved for the mass distribution $W(m,\ t)$, together with equations (2.22) and (2.23) which determine $f(t)$ and substrate concentration C_s, subject to the initial conditions

$W(m,\ o) = g(m)$, an initial mass distribution

$C(o) = \int_{0}^{\infty} mg(m)\,dm$

and $C_s(o)$ = an arbitrary initial substrate concentration.

2.5 Various Modifications of the Problem:

First, the steady state problem will be considered. Equation (2.20) is written for the steady state

$$\frac{d}{dm}\left[r(m)\ W(m)\right] = 2\int_{m}^{\infty} \Gamma(m',\ \tilde{C}_s)\ p(m,\ m')\ W(m')\,dm'$$

$$-\left[\frac{1}{\theta} + \Gamma(m,\ \tilde{C}_s)\right]\ W(m) \qquad \ldots(2.21)$$

assuming that there is no death. $mf(t)$ has been replaced by $r(m)$ where $r(m)$ is the steady state rate of mass increase for a single cell.

$$r(m) = \left[\frac{2}{R_g}\ \frac{\phi_m\ \tilde{C}_s}{\tilde{C}_s} - \mu_d\right] m \qquad \ldots(2.22)$$

$\tilde{C}_s$ is the steady state limiting substrate concentration. Substitution of (2.22) in equation (2.16) for the steady state yields

$$\left(\frac{2}{R\rho}\,\frac{\phi_m \tilde{C}_s}{K_s + \tilde{C}_s} - \mu_c\right) = \frac{1}{\theta}$$

and (2.22) becomes for the steady state

$$r(m) = \frac{m}{\theta} \qquad \ldots(2.23)$$

where θ is the holding time of the reactor. At steady state simultaneous solution of equations (2.18) and (2.19) with their left hand sides equated to zero gives the steady state substrate concentration

$$\tilde{C}_s = \frac{(1 + \theta/\mu_c)\, K_s}{\frac{2\phi_m \theta}{R\rho} - (1 + \theta\mu_c)} \qquad \ldots(2.24)$$

and the steady state biomass concentration

$$\tilde{C} = \frac{C_s^\circ - \tilde{C}_s}{\theta\left[\left(\frac{2}{R\rho}\right)\frac{\phi_m \tilde{C}_s}{K_s + \tilde{C}_s} - \gamma\mu_c\right]} \qquad \ldots(2.25)$$

It is assumed that the limiting substrate is not given off by the cell, $\gamma' = 0$.

Several interesting variations of (2.21) arise depending upon the nature of the probability functions $\phi(m, C_s)$ and $p(m, m')$

The simplest model would consider division of cells

cells dividing into daughter cells of identical mass ($m_c/2$) In such a case the probability that given a cell has divided, mass is m is $h(m) = \delta(m - m_c)$ a Dirac delta function.

$$\Gamma(m, \tilde{C}_s) = \delta(m - m_c)\, r(m, \tilde{C}_s)$$

The probability function $p(m, m') = \delta(m - \frac{m'}{2})$ equation (2.21) becomes

$$\frac{dW}{dm} = - \frac{1}{r(m, \tilde{C}_s)} \left[\frac{1}{\theta} + \frac{dr}{dm} \right] W(m) \qquad \ldots(2.26)$$

The solution (7) to (2.26) using the moment condition

$$\tilde{C} = \int_0^\infty m\, W(m)\, dm$$

to evaluate the integration constant, is

$$W(m) = \frac{\tilde{C}}{m^2 \ln 2} \qquad \frac{m_c}{2} < m < m_c$$

$$W(m) = 0 \qquad m > m_c \quad m < \tfrac{1}{2} m_c \qquad \ldots(2.27)$$

This model is a gross oversimplification.

II Cells divide on reaching a critical mass m_c, that is $\Gamma(m, C_s)$ is still a delta function, but the daughter cell masses are distributed according to

$$p(m, m') = \frac{30\, m^2\, (m' - m)^2}{m'^5} \qquad \ldots(2.14)$$

Equation (2.21) becomes in this case,

$$\frac{d}{dm}\left[W(m)\ r(m,\ \tilde{C}_s)\right] = 2\int_m^\infty r(m,\ C_s)\ \delta(m' - m_c)\ W(m')\ p(m,m')dm' - \frac{W(m)}{\Theta}$$

$$\text{or}\quad \frac{d}{dm}\left[r(m)\ W(m)\right] = 2\ W(m_c)\ p(m,\ m_c)\frac{m_c}{\Theta} - \frac{W(m)}{\Theta} \qquad \ldots(2.28)$$

Using (2.22) for r(m), an analytical solution can be written down for (2.28)

$$m^2 W(m) = m_c\ 2\ W(m_c)\int_0^m m\ p(m,\ m_c)dm \qquad \ldots(2.29)$$

Let $K_I = 2m_c\ W(m_c)$

$$W(m) = K_I\ \frac{30}{m_c 5}\left[\frac{m^4\ m_c}{4}\cdot 2 - \frac{2}{5}\ m_c\ m^5 + \frac{m^6}{6}\right]$$

on using (2.14) for $p(m,\ m_c)$ in (2.29) and integration.

The integration constant is evaluated using

$$\tilde{C} = \int_0^{m_c} m\ W(m)\ dm$$

$$K_I = \frac{2\ \tilde{C}}{37\ m_c}$$

and

$$W(m) = \frac{60\ \tilde{C}}{37\ m_c 6}\left[15\ m^2\ m_c - 24\ m_c\ m^3 + 10m^4\right]$$

$$\text{for } m \leqslant m_c \qquad \ldots(2.30)$$

$$W(m) = 0 \qquad \text{for } m > m_c$$

This solution represents a better model than I, though still an oversimplification. It is nevertheless useful in serving as a comparison with the more complicated models to be dis- [illegible] In addition it will be seen that it is a good

approximation to the actual solution of equation (2.21) in the regions of small mass where both $p(m, m')$ and $\Gamma(m, C_s)$ would be expected to be very small.

III The masses of cells at division are distributed according to equation (2.10), a Gaussian distribution. Here

$$\Gamma(m, \tilde{C}_{sk}) = \frac{2\, e^{-\left(\frac{m - m_c}{\epsilon}\right)^2}\; r(m, \tilde{C}_s)}{\epsilon\sqrt{\pi}\ \operatorname{erfc}\left(\frac{m - m_c}{\epsilon}\right)} \qquad \ldots(2.11)$$

The daughter cells are identical in mass that is $p(m, m') = (m - \frac{m'}{2})$, Equation (2.21) becomes

$$\frac{d}{dm}\, r(m)\, W(m) = 4\, \Gamma(2m)\, W(2m) - \left[\frac{1}{\theta} + \Gamma(m)\right] W(m) \qquad \ldots(2.31)$$

a functional differential equation, solutions to this equation have been presented by Eakman (7,8), by using a predictor-corrector method. The solutions to (2.31) by the method of weighted residuals followed by a successive approximation procedure will be given in Chapter IV. This model is more realistic than (1) or (2).

IV It is the object of this work to solve the most general of the above models in which distribution of cell division masses as well as distribution of daughter cell masses are considered and described by equations (2.10) and (2.14) respectively, and which will be solved in Chapter V.

by the method of weighted residuals for the steady state equation (2.21) as well as the transient equation (2.20).

2.6 Batch Propagation:

The equations of the cell model for batch propagation are obtained from (2.20), (2.18) and (2.19) by setting the dilution rate $1/\theta = 0$. The partial integro differential equation describing cell mass distribution is described by

$$\frac{\partial W}{\partial t} + \frac{\partial}{\partial m}\left[r(m, C_s)\, W(m, t)\right] = 2\int_m^\infty \Gamma(m', C_s)\, p(m, m')\, W(m', t)\, dm' - \Gamma(m, C_s)\, W(m, t) \qquad \ldots(2.32)$$

and the substrate and biomass concentrations by

$$\frac{dC_s}{dt} = \int_0^\infty \left[\alpha_\lambda'(m)\, r''(m) - \beta_\lambda'(m)\, r'(m, C_s)\right] W(m, t)\, dm \qquad \ldots(2.33)$$

$$\frac{dC}{dt} = \int_0^\infty r(m, C_s)\, W(m, t)\, dm \qquad \ldots(2.34)$$

assuming no death. (2.32) is to be solved subject to (2.33) and (2.34) and the regularity condition

$$r(\infty, C_s)\; W(\infty, t) = 0$$

2.7 Exponential Phase Propagation:

Consider a batch culture of a single species propagating in the exponential phase. If it is assumed that the substrate

concentration is sufficiently high, the changes produced by growth have no noticeable effect on the substrate concentration and hence no effect on the rate of population increase. If the culture has been growing long enough so that the cell mass distribution has become independent of time, the cell mass distribution takes the form

$$W(m, t) = N_0 \exp(\gamma t)\, \overset{*}{g}(m) \qquad \ldots(2.35)$$

where N_0 is the population density at some arbitrary zero in time in the exponential phase.

Substitution of (2.35) into the number balance (2.32) gives the integro differential equation for the asymptotic batch distribution

$$\frac{d\overset{*}{g}}{dm} = \frac{2}{r(m, C_s)} \int_m^\infty \Gamma(m, C_s)\, \overset{*}{g}(m')\, p(m, m') - \frac{1}{r(m, C_s)} \left[\Gamma(m, C_s) + \gamma + \frac{dr}{dm} \right] \overset{*}{g}(m) \qquad \ldots(2.36)$$

It is seen that equation (2.36) is exactly similar to the steady state continuous propagator population balance (2.21) except for the appearance of the term γ instead of $(1/\theta)$, substitution of (2.35) in the total number balance equation (2.2) applied to a batch system provides a relation for , the specific rate of population increase.

$$\gamma = \int_0^\infty \Gamma(m, C_s)\, \overset{*}{g}(m)\, dm \qquad \ldots(2.37)$$

To calculate ν the distribution has to be known. Therefore (2.36) and (2.37) have to be solved simultaneously for g(m) along with the normalization condition

$$\int_0^\infty g^*(m)\,dm = 1 \qquad \ldots(2.38)$$

Once again the various models discussed for the continuous propagator would be applicable here also, subject to the additional condition (2.37).

CHAPTER - III

THE METHOD OF WEIGHTED RESIDUALS (MWR)

The method of weighted residuals is one of the powerful tools used by the engineer to find approximate solutions to the equations of change of distributed systems. The approximate solutions in many cases provide a reasonable first guess that can be used in a scheme of successive approximations to obtain improved solutions. The analytical form of the solution obtained by MWR is very useful if there are many quantities of interest to be derived from the solution to the problem. The method is applicable to linear as well as nonlinear problems and requires much less computation time to generate the solution than finite difference techniques.

Collatz (18) has covered the method in detail, with many examples, applied to ordinary and partial differential equations. He calls them "error distribution" principles in accordance with the notion of distributing the error as uniformly as possible throughout the domain of the solution. Crandall(19) and Kantorovich and Krylov (20) have extensively applied the method to problems in the mechanics of solids. Finlayson and Scriven (21) have given an excellent review of the method and its application along with an exhaustive

some aspects of the method to other methods like separation of variables and variational methods has been outlined.

3.1 Basic Method for Initial Value Problems:

Let the mathematical model of a distributed system be represented by a system of differential or integro-differential equations. The boundary conditions represent the interaction of the system with its environment and the initial conditions represent some base state of interest. The general procedure in MWR is to assume a trial solution containing an arbitrary number of known functions of position and unknown functions of time. The undetermined parameters are found by substituting the trial solution into the differential equation and requiring that the error involved be distributed over the solution domain in some specified manner.

Consider the differential equation for $W(\bar{x}, t)$

$$\frac{\partial W}{\partial t} = N(W) \qquad \bar{x} \text{ in } V, \quad t > 0 \qquad \ldots(3.1)$$

where $N(.)$ denotes a general differential or differential integral operator involving spatial derivatives and integrals of W. V is the domain of interest with boundary S and t represents time. Let the initial and boundary conditions be

$$W(\bar{x}, o) = W_o(\bar{x}) \qquad \bar{x} \text{ in } V \qquad \ldots(3.2)$$

$$W(\bar{x}, t) = f_s(\bar{x}, t) \qquad \bar{x} \text{ on } S$$

Assume a trial solution of the form

$$W^*(\bar{x}, t) = \phi_s(\bar{x}, t) + \sum_{i=1}^{N} C_i(t)\, \phi_i(\bar{x}, t) \qquad \ldots(3.3)$$

where the approximating functions ϕ_i are known and satisfy the boundary conditions,

$$\phi_s = f_s \ , \quad \phi_i = 0 \quad \bar{x} \text{ on } S \qquad \ldots(3.4)$$

In this case, W^* satisfies the boundary conditions whatever $C_i(t)$ may be. The differential equation residual and the initial residual

$$R(W^*) = N(W^*) - \frac{\partial W^*}{\partial t} \qquad \ldots(3.5)$$

$$R_o(W^*) = W_o(\bar{x}) - \phi_s(\bar{x}, o) - \sum_{i=1}^{N} C_i(o)\, \phi_i(\bar{x}, o) \qquad \ldots(3.6)$$

indicate the extent to which the trial solution satisfies the differential equation. For an exact solution, the residuals vanish identically. As the number of approximating functions, N is increased, the residual could be expected to becomesmaller. The residual is made zero in an approximate sense by equating its weighted average over the whole domain to zero.

$$\langle R(W^*), \psi_j \rangle = 0 \qquad \ldots(3.7)$$

$$\langle R_o(W^*), \psi_j \rangle = 0 \qquad j = 1, 2, - - -N$$

where

$$\langle u, v \rangle = \int_V uv\, dV \qquad \ldots(3.8)$$

chosen weighting function. Equations (3.7) become a set of ordinary first order differential equations in the N unknowns $C_i(t)$ with the second of the equations providing the initial conditions $C_i(o)$.

For a linear problem $\frac{\partial W}{\partial t} = L(W)$ equations (3.7) become

$$\sum_{i=1}^{N} \frac{dC_i}{dt} \langle \psi_j, \phi_i \rangle = \sum_{i=1}^{N} C_i \langle \psi_j, L(\phi_i) \rangle + \langle \psi_j, L(W_s) \rangle \qquad \ldots(3.9)$$

or, in matrix form

$$\bar{\bar{A}} \frac{d\bar{C}}{dt} = \bar{\bar{B}} \bar{C} + \bar{b} \qquad \ldots(3.10)$$

Subject to $\bar{C}(o) = \bar{C}_o$

The solutions to this system provide the approximate solution (3.3) of the problem (3.1). Improved approximations are obtained by increasing N and their convergence should give an indication of the approach of the approximate solution to the exact solution.

In the above formulation, the boundary conditions were satisfied exactly by the trial solution and the differential equation approximately. This is called the "interior method". We speak of a "boundary method" when the trial solution satisfies the differential equation exactly but not the boundary conditions. When neither the differential equation nor the boundary condition is satisfied exactly, we have a "mixed

is made depending on the control required over the relative accuracy of the solution at various points in the region. A mixed method would allow flexibility in the choice of trial functions.

3.2 Choice of Approximating Functions ϕ_j

The choice of approximating functions is primarily dictated by the domain of interest, The functions must be linearly independent and differentiable to the extent that all terms in the differential equation and boundary conditions can be obtained. If the system of functions is complete, that is any piecewise continuous function in the domain can be approximated in the mean by an infinite linear combination of the basic functions, then convergence of the method may be expected. Mathematical proofs of convergence(20, 24, 25) are available for some problems and allow the determination of various sets of functions ϕ_j that are complete for the given problem. If the ϕ_j's are chosen as the first n members of such a set, the approximate solution must approach the exact solution as n tends to infinity. Kantorovich and Krylov (20) state that the sufficient condition for convergence to the true solution as we increase the number of trial functions is the completeness of the system of families of trial functions.

When the region of interest is finite, the ϕ_j are

members of a family of elementary functions like 1, x, x^2, ... or Sin x, Sin 2x, Sin 3x, ...etc. The choice between families rests on the nature of the problem at hand; if one were concerned with a vibration problem, it would be natural to choose the latter of the above mentioned families. Families with polynomials as members are popularly used as trial solutions. In these cases by using approximating functions which satisfy the boundary conditions and have the proper symmetry properties, accurate results can often be obtained with a very small number of functions. Snyder, Spriggs and Stewart (22) have chosen approximating functions of the form $(C^2 - x^2)$, $(C^2 - x^2)^2$, ... for obtaining velocity profiles for the steady state flow between two inclined plane walls where a boundary condition must be satisfied at $x = \pm C$. One finds this technique used very often in the Pohlhausen method of boundary-layer theory. Periodic functions have been used by Snyder and Stewart (23) to obtain velocity and pressure profiles for Newtonian creeping flow in a regular packed bed of spheres.

Very few problems have been reported in the engineering literature using MWR for an infinite or semi-infinite domain. It would seem natural to use elementary functions belonging to the family $e^{-x}\, x^n$ or e^{-nx} as approximating functions for the semi-infinite domain and $e^{-x^2}\, x^n$ or e^{-nx^2} for the infinite

Orthogonal polynomials as approximating functions are very convenient to use in many instances. For example, when one is solving for a distribution function as in the present work, expression of the trial solution in terms of orthogonal polynomials permits one to write the leading moments of the distribution straightaway in terms of the coefficients of the trial solution expansion. If a distribution W(m) can be expressed as

$$W(m) = \sum_{n=0}^{N} C_n \, p(m) \, \phi_n(m) \quad \text{where } \phi_n(m) \text{ are orthonormal}$$

polynomials with respect to a weight* function p(m), then the inner products with respect to p(m), over the domain of the distribution,

$$\begin{aligned} \langle W(m) , \phi_0(m) \rangle &= C_0 \\ \langle W(m) , \phi_1(m) \rangle &= C_1 \\ &\text{- - - - - - - - - - -} \\ \langle W(m) , \phi_N(m) \rangle &= C_N \end{aligned} \qquad \ldots(3.12)$$

$\phi_n(m)$ is an nth order polynomial and the system (3.12) can be written using the orthonormal property of ϕ_n as

$$\begin{aligned} K_{00} \mathcal{M}_0 &= C_0 \\ K_{10} \mathcal{M}_0 + K_{11} \mathcal{M}_1 &= C_1 \\ &\text{- - - - - - - - - - -} \\ \sum_{j=0}^{N} K_{Nj} \mathcal{M}_j &= C_N \end{aligned} \qquad \ldots(3.13)$$

where K_{ij} is the coefficient of m^j in $\phi_i(m)$. System (3.13) is a closed system and can be solved recursively for the moments $\mu_0, \mu_1 \ldots \mu_N$ in terms of coefficients of the trial solution C_0, C_1, C_2, $\ldots . C_N$. Alternatively, using (3.13) the trial solution (3.3) may be written in terms of moments and condition (3.7) would generate equations in the moments of the distribution. The utility of MWR seen in this regard is of immense significance to problems involving distribution functions.

Orthogonal functions suitable for the finite domain could for example be Jacobi or Legendre polynomials. For semi infinite and infinite domains, Laguerre (See Appendix A) and Hermite polynomials respectively are found suitable. The subject of orthogonal polynomials is extensively treated by Szego (27).

3.3 Choice of Weighting Functions ψ_j

The choice of weighting functions ψ_j, corresponds to various criteria in MWR.

(i) Collocation Method: The residual $R(W^*)$ in equation (3.5) is made to vanish at N collocation points. The weighting function is a Dirac delta function, $\psi_j = \delta(x_j - x)$ $j = 1$ to N. The collocation points are usually chosen at regular intervals.

A modified collocation method has been suggested by

function as well as the collocation points are determined by the orthogonality of the residual to the trial functions themselves. The method is applicable easily when the residual can be expressed as the product of a polynomial times a function. The advantage of the method is that in addition to averaging the residual to zero over the whole domain, it is made zero at the collocation points as well.

(ii) Subdomain Method: The domain of interest is divided into N sub domains and the weighting functions are

$$\psi_j = 1 \qquad \bar{x} \text{ in } V_j$$
$$= 0 \qquad \bar{x} \text{ not in } V_j$$
$$j = 1 \text{ to } N$$

As N is increased, the sub domains become smaller and smaller and the residual is approximately zero everywhere.

(iii) Least Squares Method: By choosing the weighting function

$$\psi_j = \frac{\partial R(W^*)}{\partial C_j} \qquad j = 1 \text{ to } N$$

the mean square of the residual

$$I = \int_V (R(W^*))^2 \, dV$$

is minimized with respect to the C_j.

(iv) Galerkin's Method (20): The weighting functions ψ_j are the same as the approximating functions ϕ_j. If the approximating functions are members of a complete set of

the residual orthogonal to members of the complete set. A complete set of functions has the fundamental property that a piecewise continuous function can be orthogonal to each and every member of the set only if the function is identically zero. If the approximating function and the differential equation are such that the residual is continuous, it can vanish only if it is orthogonal to each member of a complete system of functions. In practice, the residual is made orthogonal only to a finite number of the members of a complete set.

(v) Method of Moments: Galerkin's method is really a particular case of the more general method of moments in which the residual can be orthogonalized with any complete set of functions and not necessarily the trial functions themselves. Galerkin's method was singled out only because it could be related to the Rayleigh-Ritz method (20) used in solving variational problems.

The method of moments has been used throughout the present work. It was felt that a comparison of the solutions of the problem with different weighting functions would give a good indication of the error involved in the approximation. (See Chapter IV).

The special case of the method of moments with weighting functions identically equal to 1 corresponds to the Pohlhausen method of boundary layer theory.

3.4 MWR vs Other Methods for the Given Problem:

For the problem at hand MWR seems to be an ideal approach. Finite difference methods are ruled out by the infinite domain of the problem. Even if a maximum cell size can be fixed as for spherical cells and the integral term in (2.25) replaced by a finite approximating sum, the growth term has to be written using a formula from numerical differentiation. This may introduce large errors.

The method of successive approximations would require much more computational time and the final results would be in numerical form. It is difficult to predict whether the method of successive approximations would converge in the case of an infinite domain.

Using MWR, a compact analytic form of the solution could be obtained with the constants in the solution related directly to the leading moments of the distribution function in question. If sufficiently accurate results are not available, it atleast may provide a reasonable initial approximation of the solution which could be improved by successive approximations. In either case, the saving in computation time would be significant. These factors indicate that MWR represents an attractive approach to the solution of the problem.

CHAPTER - IV

SOLUTION OF POPULATION BALANCE EQUATIONS FOR A MICROBIAL PROPAGATOR USING MWR

4.1 The Steady State Propagator:

For the steady state propagator, the mass distribution is given by equation (2.20)

$$\frac{d}{dm}\left[r(m)\ W(m)\right] = 2\int_{m}^{\infty} \Gamma(m')\ p(m, m')\ W(m')\ dm' - \left[\Gamma(m) + \frac{1}{\theta}\right] W(m) \qquad \ldots(2.20)$$

The growth rate as shown earlier

$$r(m) = \frac{m}{\theta} \qquad \ldots(2.23)$$

Using (2.23), the fission probability function given by (2.11)

$$\Gamma(m, C_s) = \frac{2}{\epsilon\sqrt{\pi}} \frac{e^{-\left(\frac{m - m_c}{\epsilon}\right)^2} r(m, C_s)}{\operatorname{erfc}\left(\frac{m - m_c}{\epsilon}\right)}$$

becomes for the steady state

$$\Gamma(m) = \frac{2}{\epsilon\sqrt{\pi}} \frac{1}{\theta} \frac{m\, e^{-\left(\frac{m - m_c}{\epsilon}\right)^2}}{\operatorname{erfc}\left(\frac{m - m_c}{\epsilon}\right)} \qquad \ldots(4.1)$$

The values of the cell parameters ϵ, m_c for rod-shaped cells are taken from the work of Eakman (7) and listed in Appendix C.

For convenience in numerical computation, a change of

$$x = \frac{m}{\epsilon} \qquad \text{When } m' = m,\ y = x$$

$$y = \frac{m'}{\epsilon} \qquad \text{and as } m \longrightarrow \infty,\ x \longrightarrow \infty \qquad \ldots(4.2)$$

$$w(x) = W(\epsilon x)$$

Equation (2.20) is accordingly written as

$$\frac{1}{\theta}\frac{d}{dx}\left[xw(x)\right] = 2\int_{x}^{\infty} \Gamma(\epsilon y)\, p(\epsilon x, \epsilon y)\, w(y)\, dy - \left[\Gamma(\epsilon x) + \frac{1}{\theta}\right] w(x) \qquad \ldots(4.3)$$

Using (4.2) in Equations (4.1) and (2.14), (4.3) becomes

$$\frac{1}{\theta}\frac{d}{dx}\left[xw(x)\right] = 2\int_{x}^{\infty} \Gamma'(y)\, p'(x, y)\, w(y)\, dy - \left[\Gamma'(x) + \frac{1}{\theta}\right] w(x) \qquad \ldots(4.4)$$

where

$$\Gamma'(x) = \frac{2}{\sqrt{\pi}} \frac{e^{-(x - x_c)^2}}{\operatorname{erfc}(x - x_c)} \frac{x}{\theta} \qquad \ldots(4.5)$$

and $$p'(x, y) = \frac{30\, x^2 (y - x)^2}{y^5}, \qquad x_c = \frac{m_c}{\epsilon} \qquad \ldots(4.5a)$$

Equation (4.4) is a linear integro-differential equation in the distribution w(x). Cells with zero mass cannot exist. Therefore,

$$w(o) = o \qquad \ldots(4.6)$$

Differentiating (4.4) once with respect to x and assuming that the second derivative of w(x) is bounded at x = o, it can be established that the derivative of w(x),

$$w'(x) = o \qquad \text{at } x = o \qquad \ldots(4.7)$$

Note that $p'(o, y) = o$, as cells of zero mass cannot be formed at all. Leibnitz rule is made use of to differentiate the integral term in (4.4). It can be shown by a second differentiation of (4.4) that

$$w''(x) \neq o \qquad \text{at } x = o \qquad \ldots(4.8)$$

Assume that the distribution $w(x)$ can be expanded in the form

$$w(x) = \sum_{n=o}^{\infty} C_n \, \phi_n(x) \qquad \ldots(4.9)$$

The domain of x is $(0, \infty)$. The approximating functions $\phi_n(x)$ are chosen as

$$\phi_n(x) = e^{-x} L_n(x) \qquad \ldots(4.10)$$

where $L_n(x)$ is the nth Laguerre polynomial. For a discussion on Laguerre polynomials, see Appendix A. The family of functions (4.10) is complete in $(0, \infty)$(27) and an infinite linear combination as in (4.9) may be used to approximate $w(x)$ in $(0, \infty)$. In practice only a finite linear combination is possible. The trial solution therefore is

$$w^*(x) = \sum_{n=o}^{N} C_n \, \phi_n(x) \qquad \ldots(4.11)$$

where N is the total number of functions ϕ_n used.

Substitution of (4.11) into (4.4) gives

$$\sum_{n=o}^{N} C_n \left[\phi_n'(x) \frac{x}{\Theta} + \frac{1}{\Theta} \phi_n(x) \right]$$

$$= 2 \int_x^{\infty} \Gamma'(y)\, p'(x, y) \sum_{n=o}^{N} C_n \phi_n(y) dy$$

$$- \sum_{n=o}^{N} C_n \left[\Gamma'(x) + \frac{1}{\Theta} \right] \phi_n(x) + R(x)$$

R(x) is the residual of the integro differential equation (4.4) on using the approximation (4.11).

Letting

$$\phi_n'(x) \frac{x}{\Theta} + \frac{2}{\Theta} \phi_n(x) - 2 \int_x^{\infty} \Gamma'(y)\, p'(x,y)\, \phi_n(y) dy + \Gamma'(x)\, \phi_n(x) \equiv Fn(x) \qquad \ldots(4.12)$$

R(x) can be written as

$$R(x) = \sum_{n=o}^{N} C_n F_n(x) \qquad \ldots(4.13)$$

The residual is averaged to zero using the MWR criterion, by weighting it with members of a complete set of functions ψ_j, over the whole domain.

$$\int_o^{\infty} R(x)\, \psi_k(x) dx = 0 \qquad \ldots(4.14)$$

for k = 1, 2, ...N-2

Using (4.13), condition (4.14) is written

$$\langle R, \psi_k(x) \rangle = \sum_{n=o}^{N} \langle \psi_k(x), Fn(x) \rangle C_n = 0$$

$$\text{for } k = 1, 2, \ldots\ldots N-2 \qquad \ldots(4.15)$$

where

$\langle u, v \rangle$ denotes

in future the inner product $\int_o^\infty u(x)\, v(x)\, dx$

Defining $a_{kn} = \langle \psi_k(x), Fn(x) \rangle$, system (4.15) is written as

$$\sum_{n=o}^{N} a_{kn}\, C_n = 0 \qquad k = 1,2,,\ldots\ldots\ldots(N-2)\ldots(4.16)$$

giving (N-2) equations in (N+1) unknowns. The residual has been weighted with only (N-2) functions in order that the unknowns C_n can be made to satisfy additional conditions already known regarding the distribution. It is expected that the rise of additional information about the solution will reduce the number of approximating functions required for convergence to the final solution. Condition (4.6) applied to (4.11) yields the (N-1)th equation in the C_n's

$$w^*(o) = \sum_{n=o}^{N} C_n\, \phi_n(o) = 0 \qquad \ldots(4.17)$$

Likewise condition (4.7) becomes

$$\sum_{n=o}^{N} C_n\, \phi_n'(o) = 0 \qquad \ldots(4.18)$$

The (N +1)th equation uses knowledge of the first moment of the distribution, C given by 2.1).

The first moment of w(m) is

$$\mu_1 = \tilde{C} = \int_0^\infty m\, W(m)\,dm = \epsilon^2 \int_0^\infty xW(x)\,dx \qquad \ldots(4.19)$$

Using (4.11)

$$\tilde{C} = \epsilon^2 \int_0^\infty x \sum_{n=0}^{N} C_n \phi_n(x)\,dx$$

$$= \epsilon^2 \sum_{n=0}^{N} C_n \langle x, \phi_n(x) \rangle \qquad \ldots(4.20)$$

The orthonormal property of the approximating functions makes (4.20) an exact condition regardless of the number of approximating functions used in (4.11). The first two Laguerre polynomials are

$$L_o = 1$$

$$L_1 = (1 - x)$$

The first moment of w(m) is

$$\mu_o = \int_0^\infty w(m)\,dm = \epsilon \int_0^\infty w(x)\,dx \qquad \ldots(4.21)$$

$$= \epsilon \langle w(x),\ L_o \rangle$$

$$= \sum_{n=0}^{N} C_n \langle \phi_n,\ L_o \rangle$$

Using

$$\langle e^{-x} L_m, L_n \rangle = 0 \qquad \text{for } m \neq n$$
$$= 1 \qquad \text{for } m = n$$

$$\langle w(x), 1 \rangle = \frac{\mu_o}{\epsilon} = C_o \qquad \ldots(4.22)$$

$$\langle w(x), L_1(x) \rangle = \langle w(x), (1-x) \rangle$$
$$= \langle w(x), 1 \rangle - \langle x, w(x) \rangle$$

The left hand side $= \sum_{n=o}^{N} C_n \langle e^{-x} L_n(x), L_1(x) \rangle$

$$= C_1$$

The Right hand side $= C_o - \frac{\tilde{C}}{\epsilon^2}$, using the results (4.19) and (4.22). Therefore,

$$C_o - C_1 = \frac{\tilde{C}}{\epsilon^2} \qquad \ldots(4.23)$$

is the exact moment condition.

Equations (4.16), (4.17), (4.18) and (4.23) form the system of algebraic equations to be solved for the C_n's. It is interesting to note that the first constant C_o multiplied by the constant ϵ gives straightaway the first moment μ_o or the number of organisms in the propagator. The value of C_o as the number of trial functions is increased should approach a constant and will give an indication of the convergence of the approximation.

The system to be solved is put in matrix form

$$
\begin{bmatrix}
\langle \psi_1, F_0\rangle & \langle \psi_1, F_1\rangle & \langle \psi_1, F_2\rangle & --- & \langle \psi_1, F_N\rangle \\
\langle \psi_2, F_0\rangle & \langle \psi_2, F_1\rangle & \langle \psi_2, F_2\rangle & --- & \langle \psi_2, F_N\rangle \\
-- & -- & -- & -- & -- \\
-- & -- & -- & -- & -- \\
\langle \psi_{N-2}, F_0\rangle & \langle \psi_{N-2}, F_1\rangle & \langle \psi_{N-2}, F_2\rangle & -- & \langle \psi_{N-2}, F_N\rangle \\
\phi_0(o) & \phi_1(o) & \phi_2(o) & --- & \phi_N(o) \\
\phi_0'(o) & \phi_1'(o) & \phi_2'(o) & --- & \phi_N'(o) \\
1 & -1 & 0 & --- & 0
\end{bmatrix}
\begin{bmatrix} C_0 \\ C_1 \\ \\ \\ C_{N-3} \\ C_{N-2} \\ C_{N-1} \\ C_N \end{bmatrix}
=
\begin{bmatrix} 0 \\ 0 \\ 0 \\ 0 \\ \cdot \\ \cdot \\ \cdot \\ \frac{\tilde{C}}{\epsilon^2} \end{bmatrix}
$$

$$\text{Or} \quad \bar{A} \; \bar{C} = \bar{b} \qquad \ldots(4.24)$$

$$\bar{C}^T = (C_0, \; C_1, \; ------ \; C_N)$$

$$\bar{b} = (o, \; o, \; ------ \; C/\epsilon^2)$$

$$a_{ij} = \langle \psi_i(x), \; F_{j-1}(x)\rangle \qquad \text{for } i = 1 \text{ to } N-2$$

$$j = 1 \text{ to } N+1 \qquad (4.25)$$

$$a_{N-1,\, j} = \phi_{j-1}(o) \quad \text{for } j = 1 \text{ to } N+1 \qquad \ldots(4.26)$$

$$a_{N,j} = \phi'_{j-1}(o) \quad \text{for } j = 1 \text{ to } N+1 \qquad \ldots(4.27)$$

$$a_{N+1,\,1} = 1$$

$$a_{N+1,\,2} = -1$$

$$a_{N+1,\,j} = 0 \text{ for } j = 3 \text{ to } (N+1) \qquad \ldots(4.28)$$

Equation (4.25) is expanded, using (4.12)

$$a_{ij} = \langle \psi_i(x), \; \phi_{j-1}(x)\,\frac{x}{\theta}\rangle + \langle \frac{2}{\theta}\psi_i(x), \; \phi_{j-1}(x)\rangle$$

$$- 2\langle \psi_i(x), \; \int^{\infty} \Gamma'(y)\; p'(x, y)\; \phi_{j-1}(y)\; dy \rangle$$

The weighting functions γ_i to be used are of the form

$$\gamma_i(x) = e^{-\lambda x} x^{i-1} \quad \lambda > 0 \qquad \ldots(4.30)$$

$$\phi_{j-1}(x) = e^{-x} L_{j-1}(x) \text{ using (4.10)}$$

$L_{j-1}(x)$ is a (j-1) the order polynomial having (j-1) real distinct roots in (o, ∞). Each of the terms in (4.29), therefore corresponds to an integral having an oscillatory function as the integrand. The evaluation of such integrals poses numerical difficulties in the use of ordinary numerical integration formulae such as the Newton-Cotes formula. This difficulty is overcome for the third term for example by evaluating integrals of the form

$$\int_0^\infty e^{-\lambda x} x^{i-1} dx \int_x^\infty \Gamma'(y)\, p'(x, y) e^{-y} y^m dy \qquad \ldots(4.31)$$

which has a well behaved function for the integrand, and adding up these terms as

$$\sum_{k=1}^{j} G_{j-1,k} \int_0^\infty e^{-\lambda x} x^{i-1} dx \int_x^\infty \Gamma'(y)\, p'(x,y)\, e^{-y} y^{k-1} dy \qquad \ldots(4.32)$$

where $G_{j-1,k}$ is the coefficient of x^{k-1} in the polynomial $L_{j-1}(x)$.

Using (4.5a) for p'(x, y) and changing the order of integration, (4.32) becomes

$$\sum_{k=1}^{j} G_{j-1,k} \int_0^{\infty} \frac{\Gamma'(y)\, e^{-y} y^{k-1} dy}{y^5} \int_0^{y} e^{-\lambda x} x^{i+1} (y-x)^2 dx$$

The inner integral can be evaluated analytically. The double integral was evaluated for each k by a 32 point Gaussian quadrature formula (See Appendix B) and checked to three decimal place accuracy with the evaluation of the same by a 7 point Newton-Cotes integration formula.

Similarly, the fourth term in (4.29) is expressed as a summation of integrals

$$\sum_{k=1}^{j} G_{j-1,k} \int_0^{\infty} e^{-(\lambda+1)x} x^{i+k-1} \Gamma'(x) dx \quad \ldots(4.33)$$

A further advantage here of breaking up the function into several integrals is that only (2N-2) integrals corresponding to (2N-2) values of (i+k-1) need be evaluated as against (N-2) (N+1) integrals to be evaluated if the fourth term of (4.29) is considered as a whole for each i and j.

The first two terms of (4.29) for ψ_i given by (4.30) can be evaluated exactly by additions of integrals of the form

$$\int_0^{\infty} e^{-(\lambda+1)x} x^m = \frac{m!}{(\lambda+1)^{m+1}} \quad \ldots(4.34)$$

The matrix elements (4.25) are now known. Equation (4.24) was solved for N ranging from 4 to 18 using a matrix inversion

routine. Once the constants C_n were known the approximate solution was generated by substitution into (4.11). The results are shown in Figures (4.1) and (4.2) and discussed in Section (4.6).

4.2 Steady State Propagator, Daughter Cells of Equal Mass $m_c/2$:

This model is described by Equation (2.31), a functional differential equation

$$\frac{d}{dm}\left[r(m)\ W(m)\right] = 4\,\Gamma(2m)\ W(2m) - \left[\Gamma(m) + \frac{1}{\theta}\right] W(m) \qquad \ldots(2.31)$$

The formulation of the problem for solution is exactly the same as for the integro-differential equation, except that the double-integral term in (4.29) for the matrix element a_{ij} is replaced by the integral

$$4\left\langle \psi_i(x),\ \Gamma'(2x)\ \phi_{j-1}(2x) \right\rangle \qquad \ldots(4.35)$$

which is evaluated using Gaussian quadrature and checked by a Newton-Cotes 7 point rule. The conditions

$$w(o) = 0$$

$$w'(o) = 0$$

and knowledge of the first moment $\langle x\ w(x) \rangle$ give the last three equations of the system (4.24) as before. The results obtained are plotted in Figure (4.3) and discussed in section (4.6).

TABLE 4.1

VARIATION OF ZEROTH MOMENT OF $w(x)$, C_o WITH NUMBER OF TRIAL FUNCTIONS, N, WEIGHTING FUNCTIONS ARE OF THE FORM $e^{-\lambda x} x^n$

Number of trial functions N	C_o, Zeroth Moment x 10^{24}		
	$\lambda = 1$	$\lambda = 2$	$\lambda = 3$
4	1.5940	1.5216	1.5196
5	1.5223	1.5309	1.5085
6	1.4530	1.4713	1.4848
7	1.4483	1.4517	1.4515
8	1.4160	1.4441	1.4522
9	1.4158	1.4026	1.4333
10	1.4162	1.3643	1.4902
11	1.4150	1.3900	1.3385
12	1.4152	1.4052	1.3934

TABLE 4.2

COMPARISON OF SOLUTIONS TO THE STEADY-STATE INTEGRO DIFFERENTIAL EQUATION (2.20) FOR NO. OF APPROXIMATING FUNCTIONS N = 12.

m cell mass gm x 10^{-12}	$W(m) \times 10^{-23}$				Ratio
	Weighting Functions $e^{-\lambda x} x^n$			Final Solution after 2 successive approx. of $\lambda=1$	L.H.S. / R.H.S. for $\lambda=2$
	$\lambda = 1$	$\lambda = 2$	$\lambda = 3$		
0	0	0	0	0	1.0000
0.4	0.5449	0.4612	0.4512	0.4854	1.0002
0.8	1.3456	1.4068	1.4075	1.4861	0.9995
1.2	2.2905	2.3045	2.2945	2.4496	0.9974
1.6	3.1605	2.8687	2.9121	3.0303	0.9210
2.0	3.1845	2.9277	3.0572	3.0955	1.0328
2.4	2.4149	2.4391	2.5444	2.6578	0.6393
2.8	1.4142	1.6213	1.6067	1.5951	1.1511
3.2	0.6205	0.8085	0.6987	0.3829	1.7632
3.6	0.1639	0.2285	0.1152	0.1494	1.7631

4.3 Verification of Results Obtained by MWR by Successive Approximations:

a) Integro-Differential Equation: Equation (4.4) is written as

$$\frac{dw}{dx} + \frac{\theta}{x}\left[\frac{2}{\theta} + \Gamma'(x)\right] w(x) = \frac{2\theta}{x}\int_x^\infty \Gamma'(y)\, p'(x,y)\, w(y)\,dy \qquad \ldots(4.36)$$

The solution $w^\circ(x) = \sum_{n=0}^{N} C_n \phi_n(x)$ $\ldots(4.37)$

obtained from MWR in Section (4.2) is considered a zeroth approximation to the true solution. The first approximation $w^1(x)$ is obtained by substituting (4.37) in the right hand side of (4.36) and solving

$$\frac{dw^1}{dx} + \frac{\theta}{x}\left[\frac{2}{\theta} + \Gamma'(x)\right] w^1(x) = \frac{2\theta}{x}\int_x^\infty \Gamma'(y)\, p'(x,y)\, w^\circ(y)\,dy \qquad \ldots(4.38)$$

Equation (4.38) is an ordinary differential equation to which the solution is given by

$$w^1(x) = \int_0^x \frac{2\theta\, x''\, e^{\int_{x'}^{x''} \frac{\theta\,\Gamma'(x')dx'}{x'}}}{x^2}\, dx'' \int_x^\infty \Gamma'(y) p(x'',y)\, w^\circ(y)\,dy \qquad \ldots(4.39)$$

The integration constant equals zero since $w(o) = .o$.

For $\Gamma'(x)$ given by (4.5)

$$\int_x^{x''} \frac{\theta\,\Gamma'(x')\,dx'}{x'} = \ln\left[\frac{\operatorname{erfc}(x - x_c)}{\operatorname{erfc}(x'' - x_c)}\right] \qquad \ldots(4.40)$$

and equation (4.39) for the (n+1)th approximation, given the

nth approximation, using $p'(x, y)$ from (4.5a) becomes

$$w^{n+1}(x) = \frac{60\,\theta}{\sqrt{\pi}\,x^2}\ \mathrm{erfc}(x - x_c)\int_0^x \frac{x''^3\,dx''}{\mathrm{erfc}\,(x''-x_c)}\int_{x''}^{\infty} \Pi'(y)\,(y-x'')^2 w^n(y)\,dy \qquad \ldots(4.41)$$

The integration of the outer integral in (4.41) is done using an integration subroutine which on a single integration gives values of $w^{n+1}(x)$ for different values of x.

Two successive approximations were found to be enough for convergence to the final solution within 3 decimal place accuracy.

b) Functional Differential Equation:

The solution obtained by MWR for the functional differential equation in section (4.3) was improved upon by

$$w^{n+1}(x) = \frac{4}{x^2\sqrt{\pi}}\ \mathrm{erfc}(x - x_c)\int_0^x \frac{\Pi'(2x'')\,x''}{\mathrm{erfc}\,(x''-x_c)}\ w^n(2x'')\,dx'' \qquad \ldots(4.42)$$

derived similar to (4.41) for the integro differential equation. The zeroth approximation assumed the value zero for $W(m)$ for the region 0 to 1×10^{-12} where negative values of $W(m)$ were generated by MWR.

4.4 Use of Approximating Functions $\phi_n(x) = e^{-x} x^n$:

The approximating functions originally selected were $\phi_n = e^{-x} x^n$, which are the basic functions required to be orthogonalized in order to generate the Laguerre polynomials.

With $\phi_n = e^{-x} x^n$ the first moment condition is

$$\sum_{n=0}^{\infty} C_n \left\langle x \phi_n(x) \right\rangle = \frac{\mu_1}{\epsilon^2}$$

For a finite number of approximating functions the above condition is satisfied only approximately, becoming more and more exact as the number of trial functions is increased. So in effect, the use of approximating functions which are not orthogonal to each other results in both the differential equation and the first moment equation being satisfied only in an approximate sense. In such a case, more approximating functions are needed to generate a reasonably accurate solution. The results obtained bear this out. There was no definite trend in the improvement of the solution as the number of trial functions was increased. With the use of orthogonal polynomials as approximating functions, the moment condition became an exact one and the solution showed better convergence properties. This in addition to the fact that the moments of the distribution are directly related to the constants of the trial solution formed the basis of selection of orthogonal polynomials as approximating functions.

4.5 Use of Collocation Method for Integral Equation:

A collocation method in which the residual (4.13) was equated to zero at N points in the domain was tried first with $\phi_n(x) = e^{-x} x^n$ as approximating functions and then with

$\phi_n(x) = e^{-x} L_n(x)$. The points were chosen

a) at regular intervals

b) as zeroes of the Nth Laguerre polynomial when using $\phi_n(x) = e^{-x} L_n(x)$, n = o to N as suggested by Stewart(26).

The method failed to work in both the cases, giving erroneous results even when 25 approximating functions were used. It appears that the Collocation method is not applicable for this problem with a reasonable number of trial functions and a more elaborate procedure of averaging the error over the whole domain is required.

4.6 Discussion of Results for Steady State Solutions:

a) Integro-Differential Equation:

Three different weighting functions were considered first, of the type (4.30) with λ =1, 2 and 3. Figure (4.1) shows the variation of W(m) for different number of trial functions N for λ= 2 and θ = 2 hrs. It was observed that the solution settled down to its final values, differing only in the third decimal place with about eleven or twelve approximating functions. Table (4.1) shows the variation of the zeroth moment of W(m) given by $\in C_o$, with different N for λ= 1, 2 and 3. Figure (4.2) and Table (4.2) compare the solutions obtained for λ= 1, 2 and 3 with the number of trial functions fixed. From Table (4.2) it is seen that the solutions using weighting function $e^{-2x} x^n$ and $e^{-3x} x^n$ are closer to

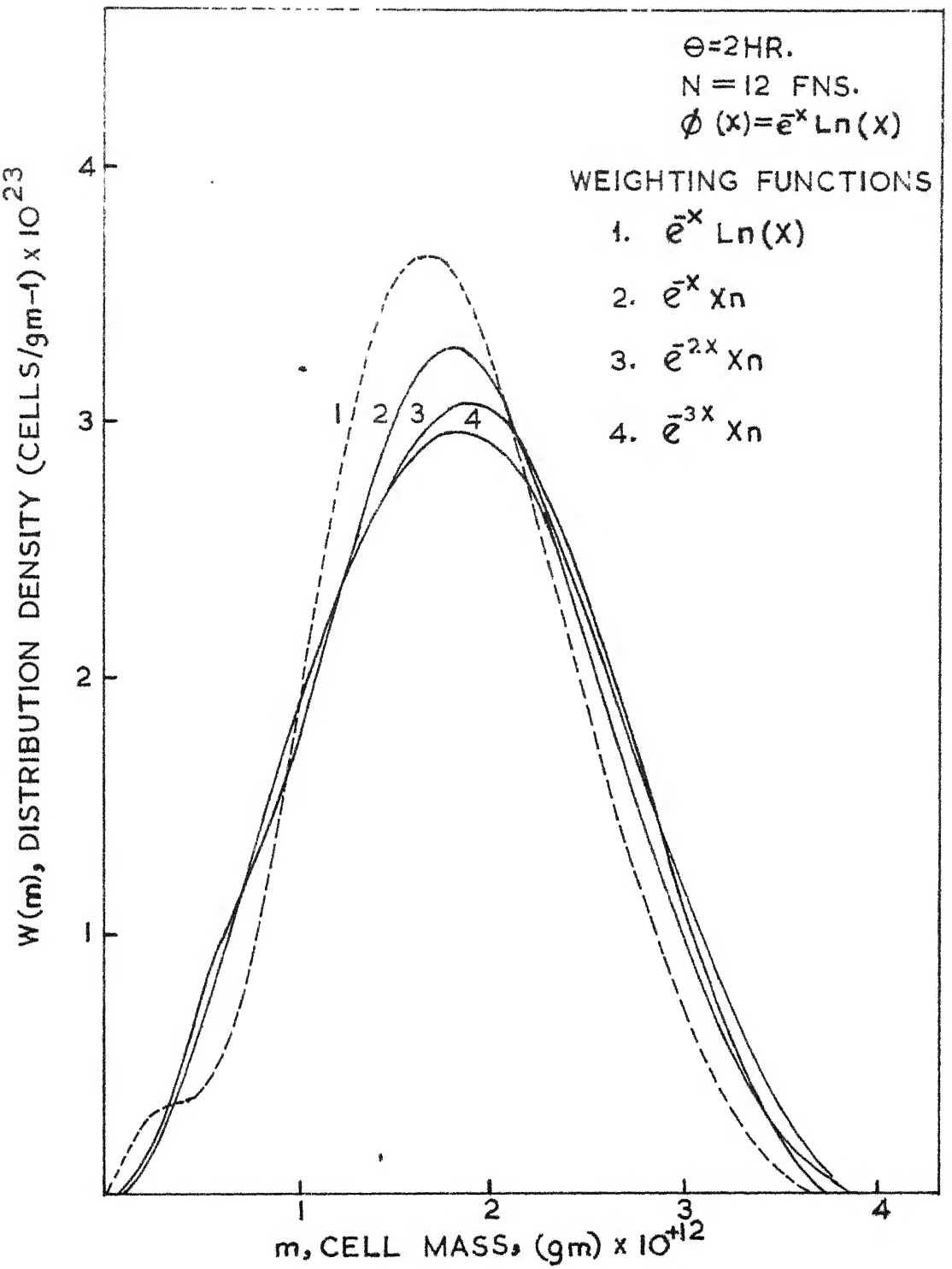


FIG.4·2 SOLUTIONS FOR STEADY STATE PROPAGATOR
COMPARISON OF WEIGHTING FUNCTIONS

the final solution than that using $e^{-x}x^n$ as a weighting function, especially in the rising portion of the solution.

Figure (4.2) includes the curve obtained by using Galerkin's method where the weighting function ψ_j is the same as the approximating function ϕ_j. In this case, both are polynomials and the integrals to be evaluated involve integrands with i+j roots, for a product $(\psi_i \cdot \phi_j)$. Thus a double summation of integrals of the form (4.31) and (4.33) is required and this was more in error as even a single summation process like (4.32) was found to involve addition and subtraction of nearly equal quantities. So one expects more deviation from the true solution for this case. These difficulties indicate that Galerkin's method is less accurate where oscillating polynomials are used as approximating functions. The error involved in the summation process increases as more trial functions are used because of the higher order polynomials so introduced. In such a situation increasing the number of trial functions may not always give an improved solution as it was observed with the Galerkin's method. In this respect, the method of moments seems superior to the Galerkin's method.

Besides observing how the solution varies with the number of trial functions and different weighting functions, an index of the extent to which the differential equation is

substituting (4.11) in (4.4) and taking the ratio of left hand side to right hand side. Table (4.2) lists these ratios at different points in the region. For values of mass upto about 2.4×10^{-12} gm (a little beyond the peak) the ratio is almost one, showing that the solution is very close to the true curve. Beyond this the ratio varies widely.

The final solution is obtained in as few as two approximations. The zeroth approximation from MWR deviates at the most by 5% from the final solution. This shows that the approximate solution is itself valuable considering that experimental results are bound to be in error atleast by this amount.

The index, ratio of the left hand side to the right hand side is not a good indicator of the correctness of the solution, especially in the region of mass beyond 2.4×10^{-12}gm. When substituting the approximate solution (4.11) in (4.3) and taking the ratio of left hand to right hand side at a particular value x_i of x, the integral term in (4.3) considers values of w(x) for x from x_i to ∞. The percentage error involved in evaluating the integral increases as x_i becomes larger as w(x) for large x_i is more in error than for small x_i. Table (4.2) reveals that the difference between the final solution and that of MWR for cell masses beyond 2.4×10^{-12} is not appreciable enough (5% deviation) to account for the

Figure (4.5) shows the variation of the distribution W(m) with holding time θ. Decreasing the holding time increases the number density of cells throughout the mass range. This is because the growth rate $r(m) = m/\theta$ and the fission probability at steady state (4.1) increase with decrease in θ, resulting in more cells of all masses. This increase more than offsets the loss due to the increase in the washout rate term $1/\theta$.

b) Functional Differential Equation:

The situation with respect to the functional differential equation is some what different. The solution generated by MWR is in great error in the region in the region of mass 0 to 1×10^{-12} gm. However, six successive approximations are sufficient to make the solution settle down to its final value. The final solution (Fig.4.3) shows that W(m) is very small (as low as 10 organisms per litre per gram) for values of mass from 0 to 1×10^{-12} gm. The maximum value of W(m) is 108 times greater than the value at $m = 1 \times 10^{-12}$ gm as contrasted with the solution of the integral equation where it is only four times the value. The nature of the solution compares well with that obtained by Eakman(8).

One may conclude from this that it is difficult for MWR to generate such a solution peculiar to the functional differential equation. At the most it may provide a rough guess of the solution in some regions. It may be difficult

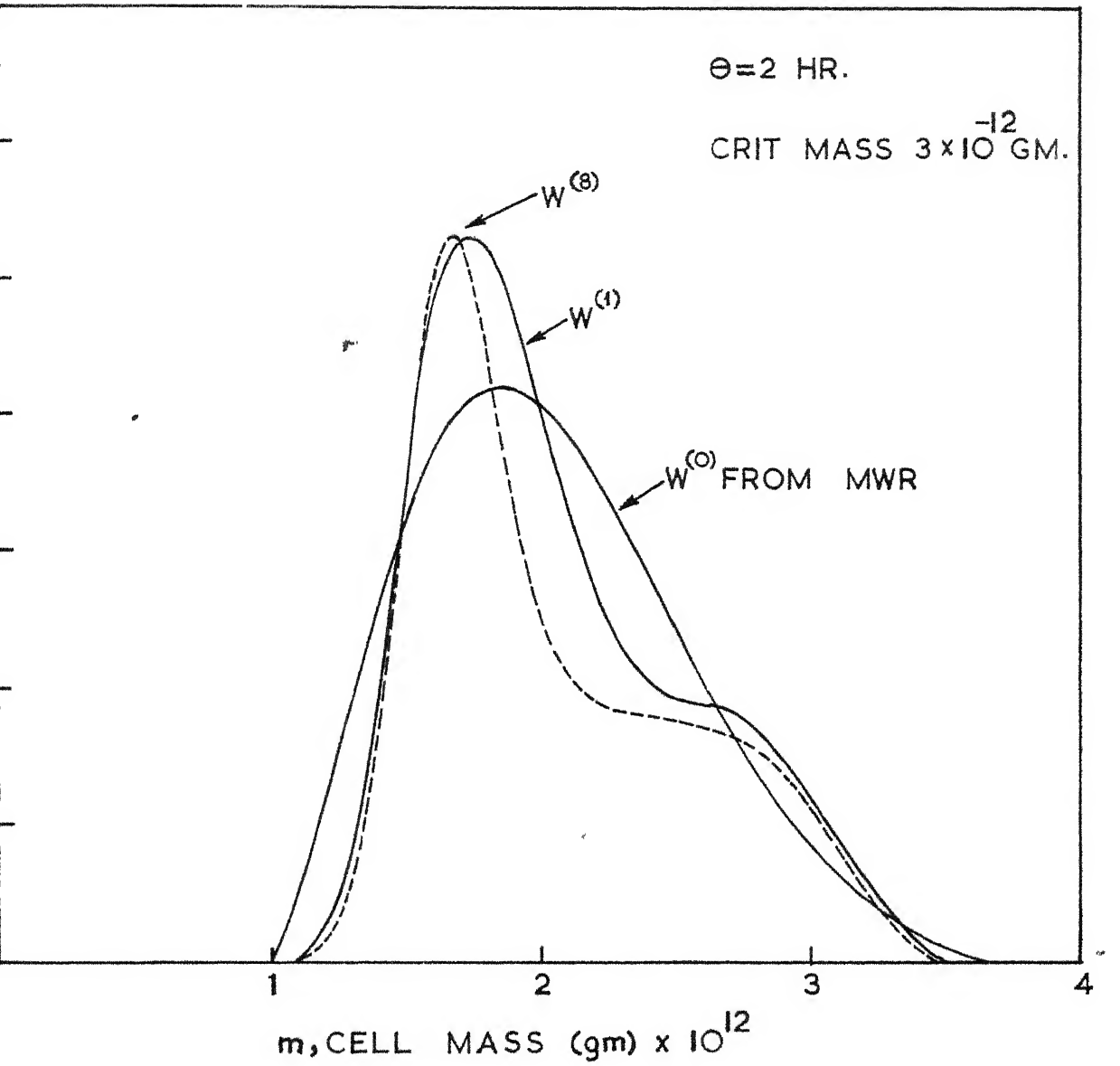
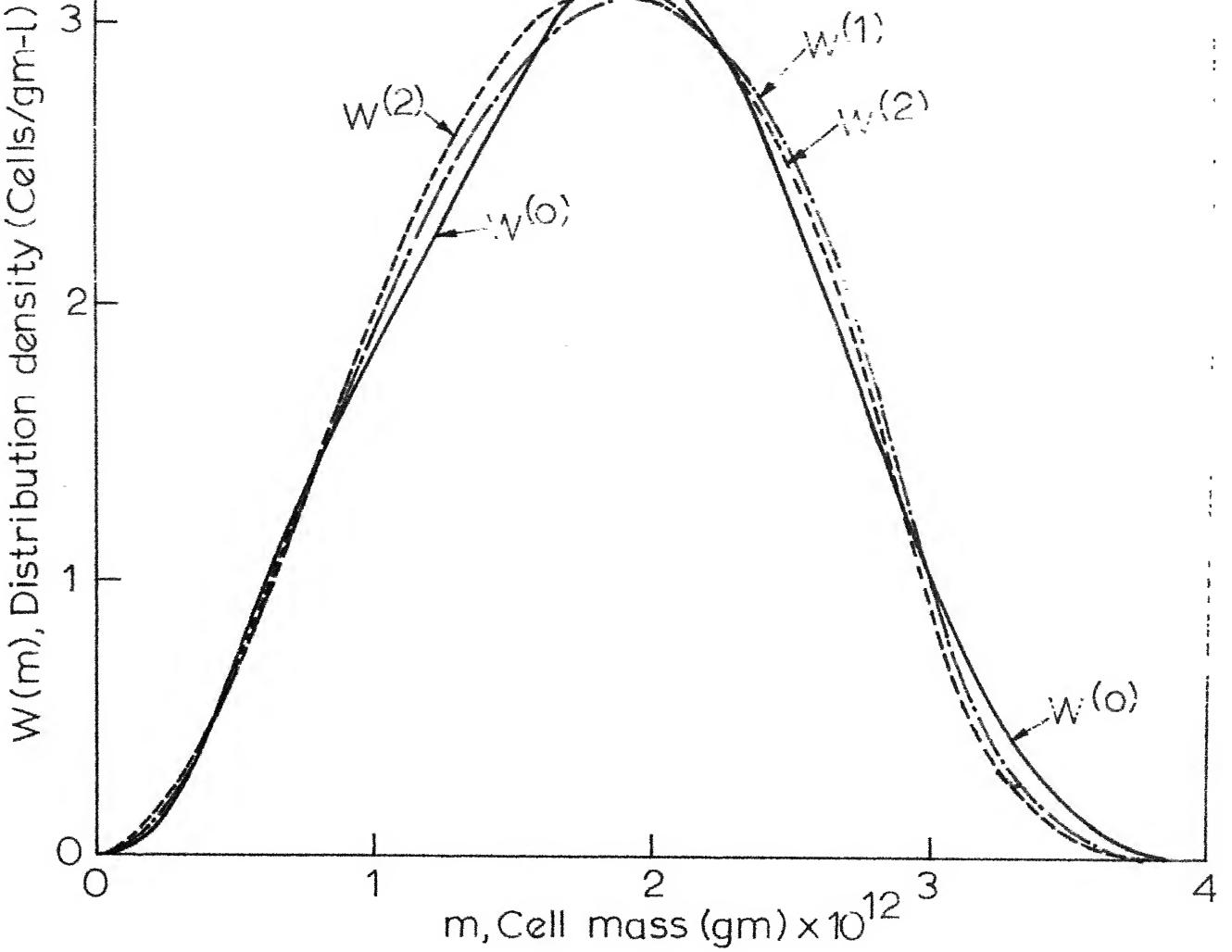
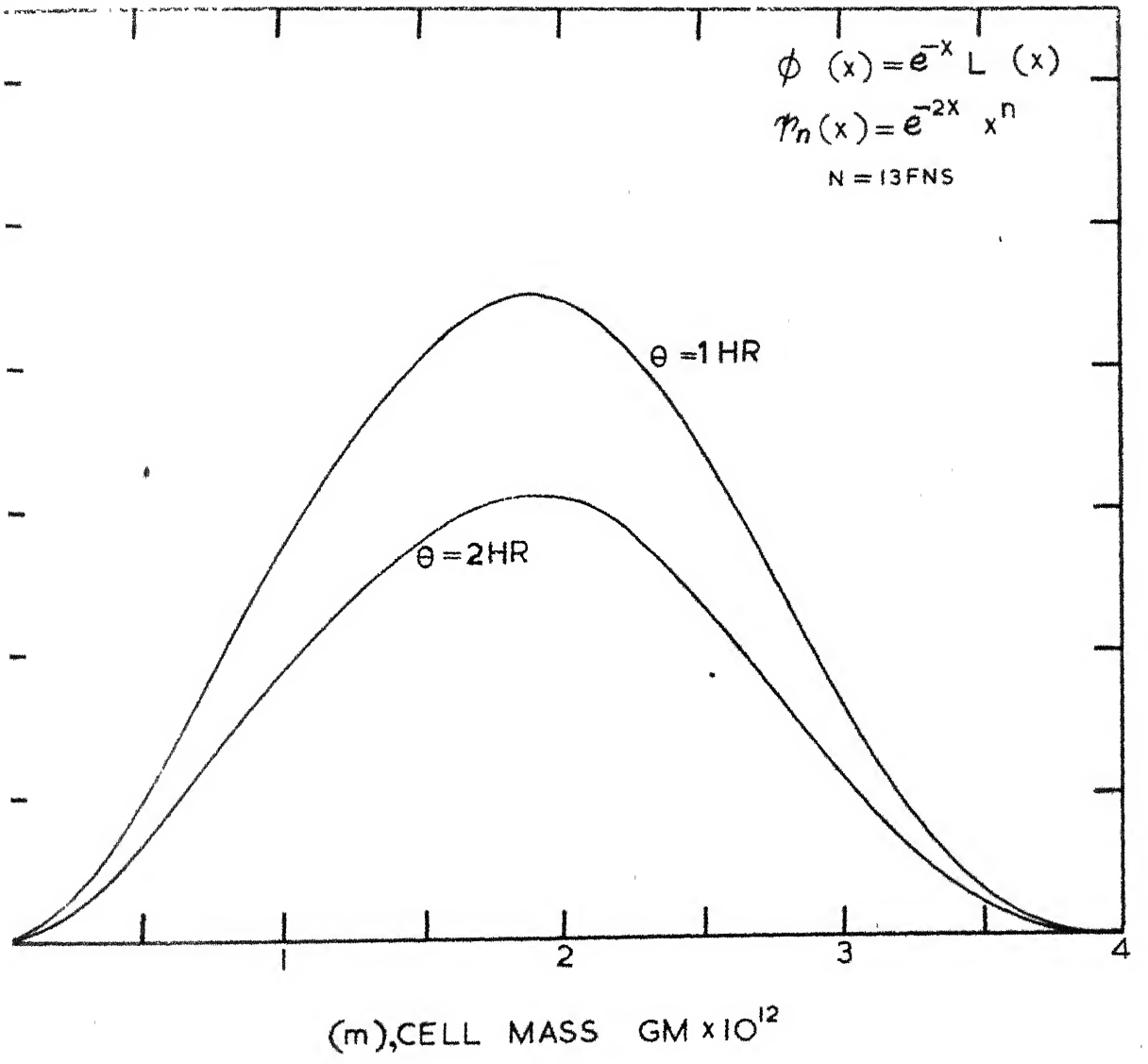


FIG. 43 METHOD OF SUCCESSIVE APPROXIMATIONS FOR THE FUNCTIONAL DIFFERENTIAL EQUATION



Method of successive approximations for steady state integro differential equation.

Fig.4.4



5 STEADY STATE CELL MASS DISTRIBUTION FOR DIFFERENT HOLDING TIMES

for a linear combination of a small number of polynomials like (4.11) to generate a solution of such wide variations in its magnitude.

c) Comparison of Models:

Figure (4.6) compares the results for the three models described in section(2.5) by Equations (2.28), (2.31) and (2.21). The general model IV (2.21) gives results close to those of model III in the region of small mass. This is to be expected since $\Gamma'(m)$ is very small for small m Fig.(4.7). $\Gamma'(m)$ is zero for model III till $m = m_c$ where it is infinite. It does have a finite value and this accounts for the curve for model IV being above that of model III in the regions of small mass.

Fig. (4.7) shows that $\Gamma'(m)$ starts rising steeply after $m = 2 \times 10^{-12}$ gms. This indicates that very few of the dividing cells have masses below 2×10^{-12} gms. Thus if one assumes that cells divide exactly into two halves, there will be very few cells with masses below 1×10^{-12} gms as shown by the final solution to the function differential equation (2.31)

The integro-differential equation considers a distribution of daughter cell masses and so one can expect more cells of small mass in this model.

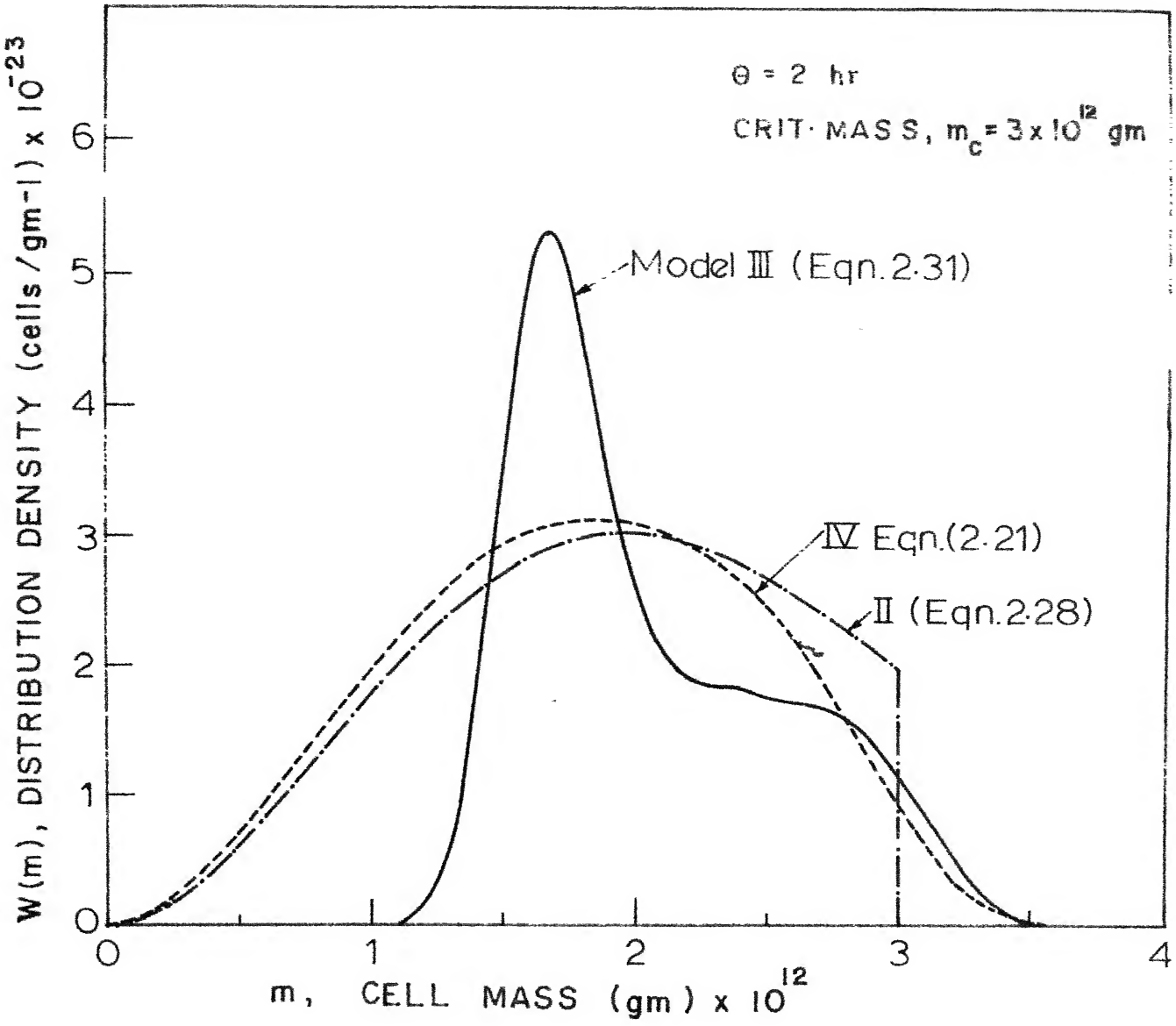
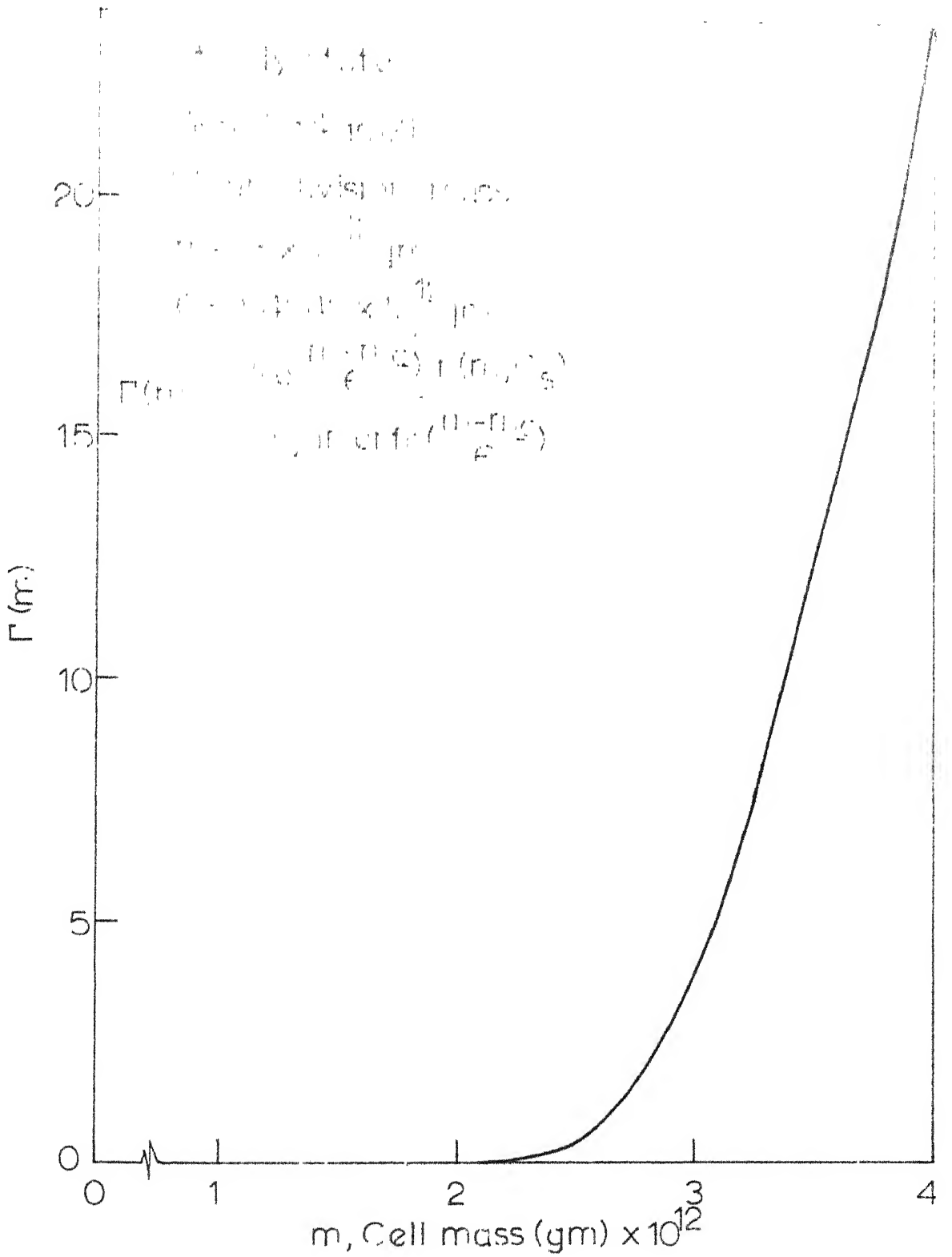

θ = 2 hr
CRIT· MASS, $m_c = 3 \times 10^{12}$ gm
Model III (Eqn. 2·31)
IV Eqn.(2·21)
II (Eqn.2·28)
W(m), DISTRIBUTION DENSITY (cells/gm-1) x 10^{-23}
m, CELL MASS (gm) x 10^{12}
0
1
2
3
4
5
6

Fig. 4.6


Γ(m)
20
15
10
5
0
0
1
2
3
4
m, Cell mass (gm) x 10^12

4.7 The Unsteady State Propagator:

The partial integro-differential equation describing the mass distribution of cells in the unsteady state (2.20) is

$$\frac{\partial W}{\partial t} + \frac{\partial}{\partial m}\left[r(m, C_s)\, W(m,t)\right] = 2\int_m^\infty \Gamma(m', C_s)\, p(m,m') W(m',t)\, dm' - \left[\Gamma(m, C_s) + \frac{1}{\theta}\right] W(m, t) \qquad \ldots(2.20)$$

$$r(m, C_s) = \left[\frac{2}{R\rho}\,\frac{\phi_m\, C_s(t)}{K_s + C_s(t)} - \mu_c\right] m$$

$$= f(t)\, m \qquad \ldots(2.15)$$

Changing the independent variable according to

$$m = \epsilon x, \quad m' = \epsilon y$$

(2.20) is written

$$\frac{\partial w}{\partial t} + f(t)\,\frac{\partial}{\partial x}\left[x\, w(x, t)\right] = 2\int_x^\infty \Gamma'(y,t)\, p'(x,y)\, w(y,t)\, dy - \left[\Gamma'(x, t) + \frac{1}{\theta}\right] w(x, t) \qquad \ldots(4.43)$$

$W(m, t) = W(\epsilon x, t) = w(x, t)$

$p'(x, y)$ is given by (4.5a)

$$\Gamma'(x, t) = \frac{2}{\epsilon\sqrt{\pi}}\,\frac{e^{-(x - x_c)^2}}{\operatorname{erfc}(x - x_c)}\, f(t)\, x \qquad \ldots(4.44)$$

On using (2.15) and $\frac{m_c}{\epsilon} = x_c$ in (2.11)

Equation (4.43) is re-arranged in the form

$$\frac{\partial w}{\partial t} = -f(t)\, x\,\frac{\partial w}{\partial x} + 2\int_x^\infty \Gamma'(y,t)\, p'(x,y)\, w(y,t)\, dy$$

where L is an integro-differential operator such that

$$Lv = - f(t)\, x \frac{\partial v}{\partial x} + 2 \int_x^\infty \Gamma'(y,t)\, p'(x,y)\, v(y)\, dy - \left[\Gamma'(x,t) + \frac{1}{\theta} + f(t)\right] v(x) \qquad \ldots(4.46)$$

Assume that the solution to (4.43) is of the form

$$w^*(x,t) = g(x) + \sum_{n=o}^{N} C_n(t)\, \phi_n(x) \qquad \ldots(4.47)$$

where $w^*(x, o) = g(x)$ $\qquad \ldots(4.48)$

with $C_n(o) = o$ for $n = o$ to N

ϕ_n are the orthonormal system of Laguerre polynomials as before.

The selection of the form of (4.47) merits attention. An expression of the type $\sum C_n \phi_n(x)$ simplifies the selection of trial functions. Solutions based on

$$w^*(x,t) = \sum_{n=o}^{N} C_n(t)\, \phi_n(x)$$

can resolve the time dependent behaviour more completely since the errors can be orthogonalized at every instant of time instead of being orthogonalized over a finite period of time. Also in most problems a smaller set of functions may be used because the ϕ_n's do not depend on t.

Condition (4.48) ensures that the initial residual

$$w^*(x,o) - g(x) - \sum_{n=o}^{N} C_n(o)\, \phi_n(x)$$

is exactly zero.

Substituting the trial solution $w^*(x, t)$ in (4.45)

$$\frac{\partial w^*}{\partial t} = \sum_{n=o}^{N} C_n'(t)\, \phi_n(x) = L\left[g(x) + \sum_{n=o}^{N} C_n(t)\, \phi_n(x)\right]$$

The residual $R(x, t)$ of the equation (4.45) is

$$\sum_{n=o}^{N} C_n'(t)\, \phi_n(x) - Lg(x) - \sum_{n=o}^{N} C_n(t)\, L\phi_n(x) \qquad \ldots(4.49)$$

The MWR criterion

$$\int_o^\infty R(x, t)\, \psi_j(x)\, dx = 0 \qquad \ldots(4.50)$$

$$j = 1 \text{ to } N-1$$

of weighting the residual with members of a complete set of functions ψ_j, gives the system

$$\sum_{n=o}^{N} \frac{dC_n}{dt} \langle \phi_n, \psi_j \rangle = \langle Lg(x), \psi_j \rangle + \sum_{n=o}^{N} C_n \langle L\phi_n(x), \psi_j \rangle \qquad \ldots(4.51)$$

$$j = 1 \text{ to } N-1$$

Weighting has been done with $(N-1)$ functions only, so that the known condition

$$w(o, t) = o \quad \text{for all } t \qquad \text{----- (4.52)}$$

and knowledge of the first moment of the distribution from (2.18) and (2.19) may be used.

It is to be noted that a condition corresponding to (4.7) regarding the derivative of the distribution respect to x at

$x = o$ does not exist in the unsteady state. Differentiating (4.43) partially with respect to x and assuming that the second partial derivative $\frac{\partial^2 w}{\partial x^2}$ at $x = o$ is bounded, the following condition is arrived at

$$\frac{\partial w}{\partial x}\Big|_{x=o} \left[2 f(t) + \frac{1}{\theta} \right] = - \frac{\partial^2 w}{\partial x \partial t}\Big|_{x=o} \qquad \ldots(4.53)$$

The right hand side of (4.53) need not in general be zero, and $\frac{\partial w}{\partial x}$ is therefore not zero at $x = o$.

Condition (4.52) provides the Nth equation in C_n

$$g(o) + \sum_{n=o}^{N} C_n(t)\, \phi_n(o) = o$$

or in terms of derivatives with respect to t of C_n's

$$\sum_{n=o}^{N} C_n'(t)\, \phi_n(o) = o \qquad \ldots(4.54)$$

The (N+1)th equation is derived making use of the moment condition

$$\int_o^\infty w(x,t)\ .1.\ dx = \frac{\mu_o(t)}{\epsilon} \qquad \ldots(4.55)$$

$\mu_o(t)$ is the number density of organisms in the propagator at time t. Using (4.47) for $w(x,t)$ in the left hand side of (4.55)

$$\int_o^\infty w(x,\ t)\ L_o(x)dx = \langle g(x), 1 \rangle + \sum_{n=o}^{N} C_n \langle \phi_n, L_o \rangle$$

by orthogonality property of L_n. Similarly,

$$\int_0^\infty w(x,t)\, L_1(x)\,dx = \langle w(x,t), (1-x) \rangle = \frac{\mu_0(t)}{\epsilon} - \frac{\mu_1(t)}{\epsilon^2} \qquad \ldots(4.5$$

Also

$$\int_0^\infty w(x,t)\,(1-x)\,dx = \langle g(x), (1-x) \rangle + \sum_{n=0}^{N} C_n \langle \phi_n(x), L_1(x) \rangle$$

Thus

$$\frac{\mu_0(t)}{\epsilon} - \frac{\mu_1(t)}{\epsilon^2} = \langle g(x), (1-x) \rangle + C_1(t) \qquad \ldots(4.5$$

Using (4.56) for $\frac{\mu_0}{\epsilon}$ equation (4.58) gives

$$C_0(t) - C_1(t) = -\langle x, g(x) \rangle + \frac{C(t)}{\epsilon^2} \qquad \ldots(4.5$$

$C(t)$ is the first moment $\mu_1(t)$ and represents the biomass concentration.

Differentiating (4.59) with respect to t

$$C_0'(t) - C_1'(t) = \frac{1}{\epsilon^2} \frac{dC(t)}{dt} \qquad \ldots(4.6$$

is the (N+1)th equation to be used.

$\frac{dC(t)}{dt}$ is obtained at any time from the simultaneous solution of (2.18) and (2.19)

$$\frac{dC}{dt} = -\frac{C}{\theta} + \left(\frac{2}{R\rho} \frac{\phi_m C_s}{K_s + C_s} - \mu_c\right) C \qquad \ldots(2.1$$

$$\frac{dC_s}{dt} = \frac{(C_s^\circ - C_s)}{\theta} - \frac{2\beta}{R\rho} \frac{\phi_m C_s C}{K_s + C_s} \qquad \ldots(2.1$$

Equations (4.51), (4.54), (4.60), (2.18) and (2.19) are to be solved simultaneously for $C(t)$, $C_s(t)$ and the $N + 1$ variables C_o, $C_1(t) \ldots C_N(t)$. The forms of the terms in the system of equations (4.51) will be examined. The second term on the right hand side is got by summing integrals of the type

$$\begin{aligned} &\langle L\, \phi_n(x), \psi_j \rangle \\ &= - f(t) \left\langle x\, \phi_n'(x), \psi_j(x) \right\rangle \\ &\quad + \left\langle \psi_j(x),\ 2 \int_x^\infty \Gamma'(y, t)\, p'(x, y)\, \phi_n(y)\, dy \right\rangle \\ &\quad - \left\langle \Gamma'(x, t)\, \phi_n(x), \psi_j(x) \right\rangle \\ &\quad - \frac{1}{\theta} \left\langle \phi_n(x), \psi_j(x) \right\rangle \\ &\quad - f(t) \left\langle \phi_n(x), \psi_j(x) \right\rangle \end{aligned} \qquad \ldots(4.61)$$

The first term on the right hand side is

$$\left\langle Lg(x), \psi_j \right\rangle$$

which is of the same form as (4.61) with $g(x)$ replacing $\phi_n(x)$. Examination of (4.61) reveals that the form of the integrals to be evaluated numerically corresponds to the type given by (4.32) if one uses weighting functions of the form $e^{-\lambda x} x^n$. This is so because $\Gamma'(y, t)$ is expressible as (4.44) where the function of time can be separated out and the remaining portion is a function of x only. Thus there is no need to evaluate integrals other than that used for the steady state solution.

Define.

$$M(x) = \frac{e^{-(x - x_c)^2}}{\operatorname{erfc}(x - x_c)} \frac{2}{\sqrt{\pi}} \qquad \ldots(4.62)$$

and

$$H_n(x) = x\,\phi_n'(x) - 2\int_x^{\infty} M(y)\,yp'(x,y)\,\phi_n(y)\,dy$$

$$+ x\bar{M}(x)\,\phi_n(x) + \phi_n(x)$$

The second term on the R.H.S. of (4.51) is now

$$-f(t)\sum_{n=o}^{N} C_n\left[\left\langle H_n(x), \psi_j(x)\right\rangle\right] - \frac{1}{\theta}\sum C_n\left\langle \phi_n, \psi_j\right\rangle$$

$$j = 1 \text{ to } N-1 \qquad \ldots(4.63)$$

The system of equations (4.51) (4.54) and (4.60) is expressed as a matrix differential equation, using (4.63).

$$\bar{\bar{A}}\,\frac{d\bar{C}}{dt} = -f(t)\,\bar{\bar{B}}\,\bar{C} - \frac{1}{\theta}\,\bar{\bar{D}}\,\bar{C} + f(t)\,\bar{w}$$

$$- \frac{1}{\theta}\,\bar{v} + \bar{t} \qquad ; \qquad \ldots(4.64)$$

where $\bar{C} = (C_o(t), C_1(t) - - - - - - C_N(t))$

$$\bar{\bar{A}} = \begin{vmatrix} \langle \phi_o, \psi_1\rangle & \langle \phi_1, \psi_1\rangle & \langle \phi_2, \psi_1\rangle \cdots \langle \phi_N, \psi_1\rangle \\ \langle \phi_o, \psi_2\rangle & \langle \phi_1, \psi_2\rangle & \langle \phi_2, \psi_2\rangle & \langle \phi_N, \psi_2\rangle \\ - \\ - \\ \langle \phi_o, \psi_{N-2}\rangle & \langle \phi_1, \psi_{N-2}\rangle & \langle \phi_2, \psi_{N-2}\rangle & \langle \phi_N, \psi_{N-2}\rangle \\ \phi_o(o) & \phi_1(o) & \phi_2(o) & \phi_N(o) \\ 1 & -1 & 0 - - - - - -0 \end{vmatrix}$$

$\bar{\bar{D}}$ is a matrix with elements

$$d_{ij} = a_{ij} \qquad \text{for } i = 1 \text{ to } N-1, \quad j = 1 \text{ to } N+1$$

$$d_{ij} = 0 \qquad \text{for } i = N, N+1, \quad j = 1 \text{ to } N+1$$

$$\bar{\bar{B}} = \begin{bmatrix} \langle H_0(x), \psi_1(x)\rangle & \langle H_1(x), \psi_1(x)\rangle \cdots & \langle H_n(x), \psi_1(x)\rangle \\ \langle H_0(x), \psi_2(x)\rangle & \langle H_1(x), \psi_2(x)\rangle \cdots & \langle H_n(x), \psi_2(x)\rangle \\ \cdots & \cdots & \cdots \\ \cdots & \cdots & \cdots \\ \langle H_0(x), \psi_{N-2}(x)\rangle & \langle H_1(x), \psi_{N-2}(x)\rangle \cdots & \langle H_n(x), \psi_{N-2}(x)\rangle \\ 0 & 0 \cdots & 0 \\ 0 & 0 \cdots & 0 \end{bmatrix}$$

The general term for $i = 1$ to $N-2$, $j = 1$ to $N+1$, $\langle H_{j-1}(x), \psi_i(x)\rangle$ requires only the integrals used in the steady state problem.

$\bar{w}$ is a vector such that

$$w_k = -\langle g'(x)x, \psi_k(x)\rangle + \left\langle \psi_k(x) ; 2\int_x^\infty yM(y)p'(x,y)\, g(y)\, dy \right\rangle - \langle x\, M(x)\, g(x), \psi_k(x)\rangle - \langle g(x), \psi_k(x)\rangle \quad \ldots(4.65)$$

for $k = 1$ to $N-1$.

$$w_N = w_{N+1} = 0$$

$\bar{V}$ is a vector such that

$$v_k = \langle g(x), \psi_k(x)\rangle \text{ for } k = 1 \text{ to } N-1 \quad \ldots(4.66)$$

$\bar{t}$ is a vector such that

$$t_k = 0 \quad \text{for } k = 1 \text{ to } N$$

$$t_{N+1} = \frac{1}{\epsilon^2} \frac{dC(t)}{dt}$$

$C(t)$ is the biomass concentration at time t.

Multiplying (4.64) throughout by $\bar{\bar{A}}^{-1}$

$$\frac{d\bar{C}}{dt} = - f(t)\, \bar{\bar{A}}^{-1} \bar{\bar{B}}\, \bar{C} - \frac{1}{\theta}\, \bar{\bar{A}}^{-1} \bar{\bar{D}}\, \bar{C}$$

$$+ f(t)\, \bar{\bar{A}}^{-1} \bar{w} - \frac{1}{\lambda}\, \bar{\bar{A}}^{-1} \bar{v} + \bar{\bar{A}}^{-1} \bar{t} \qquad \ldots(4.67)$$

which are a set of first order ordinary differential equations to be solved for $\bar{C}$ simultaneously with (2.18) and (2.19) which determine $C(t)$, $C_s(t)$ and hence $f(t)$ in (4.67). The initial conditions are $\bar{C}(o) = \bar{o}$ and

$$C(o) = \int_o^\infty g(m)\, dm = \epsilon \left\langle g(x), 1 \right\rangle$$

and $C_s(o)$ is specified arbitrarily.

The system of equations (4.67) together with (2.18) and (2.19) was integrated using a Runge-Kutta-Gill method. The solutions were obtained for the following types of initial distributions:

a) $g(x) = k\, x\, e^{-x} \cdot 10^{24}$, a population consisting of predominantly cells of small mass. Two values of k were used. The results are presented in figures (4.10), (4.11), (4.13) and (4.14) for approximating functions $\phi_n = e^{-x} L_n(x)$ and weighting functions of the type $\chi(x) = e^{-\lambda x} x^n$

b) $g(x) = k\, x^5\, e^{-x}$, 10^{24}, a population consisting of predominantly cells of large mass. The solution is shown in Figure (4.12)

Figure (4.8) compares the solutions obtained at a particular time as the number of trial functions is increased. Figure (4.9) shows the effect of using different weighting functions, for the same number of approximating functions. The results are discussed in section (4.8).

4.8 The Batch Propagator:

a) Changing Environment: The cell mass distribution of batch culture in a changing environment was obtained by solution of equation (2.32) by MWR. The formulation of the method of solution is the same as for the continuous propagator equations but for the omission of the (1/θ) term in (2.20) (2.18). The system of differential equations to be solved now is

$$\bar{\bar{A}}\,\frac{d\bar{C}}{dt} = -\,f(t)\,\bar{\bar{B}}\,\bar{C} + f(t)\,\bar{w} + \bar{t} \qquad \ldots(4.68)$$

$$f(t) = \left[2\,\frac{\phi_m}{R\rho}\,\frac{C_s(t)}{[K_s + C_s(t)]} - \mu\right] \text{ as before}$$

$$\frac{dC}{dt} = \left[2\,\frac{\phi_m}{R\rho}\,\frac{C_s}{(K_s + C_s)} - \mu_c\right] C \qquad (2.33)$$

$$\frac{dC_s}{dt} = -\,2\,\frac{\phi_m}{R\rho}\,\beta\,\frac{C_s C}{(K_s + C_s)} \qquad (2.34)$$

subject to

$$\bar{C}(o) = \bar{O}$$

$$C(o) = \int_o^\infty g(m)\,dm \qquad \text{where}$$

$w(m, o) = g(m)$ an initial distribution on and $C_s(o)$ is an arbitrary initial substrate concentration.

The results obtained are presented in Figure (4.16).

b) Exponential Batch Growth:

Considering the environment to be essentially constant the distribution of cell masses is obtained as in (a), but omitting the substrate balance (2.33) and assuming C_s a constant in (2.34). The exponential growth phase is shown by the straight line portion of the plot of ln N against time in Figure (4.18). Exponential batch growth mass distribution can be written as

$$W(t, m) = N_o \exp(\lambda t) \quad g^*(m) \qquad \ldots(2.35)$$

Knowledge of λ from the slope of the straight line portion of Figure (4.18) allows calculation of $g^*(m)$ from $w(m, t)$.

Equation (2.36) for $g^*(m)$ was solved independently by MWR similar to the solution of the steady state propagator balance (2.21) but using $\int_o^\infty g^*(m)dm = 1$ instead of the moment condition (4.23) and the value of obtained earlier. The solutions for $g^*(m)$ by the two methods were in good agreement (Fig. 4.19). An initial distribution of the type $W(x, o) = xe^{-x}$ was assumed.

4.9 Discussion of Results for the Unsteady State Equation:

a) Test of Correctness of the Solutions:

Whatever the type of initial distribution chosen, the unsteady state solution approached the steady state solution determined independently, to a good degree of accuracy. This is only a necessary but not sufficient condition for the correctness of the solution. However, several factors, discussed below, provide reasonable bases for assuming that the solutions were correct. These factors relate to,

1. Noting the rate of convergence of the solution at any fixed time co-ordinate by increasing the number of approximating functions. About ten functions were found enough to give a solution which did not change appreciably on further addition of trial functions. This conclusion applies also to convergence of the first moment of W(m, t) to its final value.

2. Solving the problem for different weighting functions Three different weighting functions were used. For the same number of approximating functions, the different weighting functions gave reasonably close solutions at any time, The variation between the results was at most 5%.

3. Solving the problem for a situation where the nature of the solution is known definitely. Batch growth under constant environment was treated as a special case of the general problem. The solutions obtained fitted very well with

the exponential phase mass distribution $W(m, t) = N_o e^{\lambda t} g^*(m)$. On using the value of λ obtained from this fit, in the integro-differential equation for $g^*(m)$ and solving it, the distribution obtained corresponded to that got by the relation

$$g^*(m) = \frac{W(m, t)\, e^{-\lambda t}}{N_o}$$

b) Interpretation of the Results for a Continuous Propagator

1. Figure (4.11) shows that for an initial distribution having comparatively larger number of cells of small mass, the total number density in the propagator N(t) decreases first. This can be interpreted by saying that the probability of small cells dividing is small and thus in the initial stages the loss in number by washout is significant compared to the term accounting for gain by division. Starting with zero substrate in the reactor, one finds that growth is also slow initially and the substrate concentration at the outlet of the reactor rises to a maximum value. By this time the cells have grown enough to start multiplying by division. Rapid increase in the number of cells increase the rate of consumption of substrate which starts dropping down rapidly.

The distribution (Fig. 4.10) follows the behaviour of the first moment which is determined independently here. Although initially the number density decreases, the first moment does not, because of the formation of more cells of large mass by

the propagator as well as the biomass concentration is brought about by division of larger cells. As a result, substrate is consumed very rapidly and the biomass concentration and number density overshoot the steady state value. The steady state is reached in about three hours.

2. An initial cell mass distribution of very few cells mostly of small mass takes a much longer time to assume the steady state distribution. (Figures(4.13) and (4.14)). The number of density and mass distribution change with time similar to case (1) but the initial drop in the number of cells is not as significant as in (1) because there are very few cells totally.

3. An initial distribution with cells of relatively large mass changes in time as shown in Figures (4.12) and (4.14). The number of cells of smaller mass starts increasing as a result of division of large cell and the entire curve shifts towards the left to the steady state value. Accordingly the total number of cells N rises steeply at first and settles down to its final value. The steady state is reached much faster compared to cases (1) and (2) since the initial distribution is closer to the steady state distribution than case (1) or case (2).

c) Results for the Batch Propagator:

1. Changing Environment:

The mass distribution for a batch propagator is shown in Figure (4.17). The biomass concentration c, the substrate concentration C_s and the number density N, vary with time as shown in Figure (4.1[illegible]). It is seen that after about 0.5 hrs the substrate concentration decreases to very small values, the point at which the biomass concentration starts dropping rapidly. The growth rate becomes nagative in the particular model used. The transition probability of cell division as in (2.11) would then become negative which is impossible physically. It can be shown (32) that

$$r\,(m,\ C_s)$$

should be replaced by $|r(m,\ C_s)|$ in the expression (2.11).

A negative growth rate would reduce the number of cells of large mass, and increase the number of cells of small mass (see Figure (4.16)). The total number of cells eventually becomes constant as no death has been assumed and it is more difficult for smaller cells to divide.

2. Constant Environment:

The solutions for constant environment fit very well with the expected form of number increase $N(t) = N_o\, e^{\nu t}$. After an initial adjustment period the plot of Log N. vs time (Fig. 4.18) is a straightline representing exponential growth,

in exponential growth. The asymptotic mass distribution g(m) calculated from W(m, t) on solution of (2.32) directly with C_s constant is nearly identical to that obtained by solving the integro-differential equation (2.36) for g(m) with $\lambda = 1.282$ (Figure (4.19)).

d) Numerical Difficulties Involved in the Solution of System (4.67):

For the approximating function family $\phi_n(x) = e^{-x} L_n(x)$ and weighting function family $\psi_n(x) = e^{-x} x^n$ it was found that the system of equations became difficult to solve for matrices larger than order 7. The matrix $\bar{\bar{A}}$ was such that its inverse contained large elements and extremely fine interval were required in the Runge-Kutta method for the solution to remain stable. This trouble did not arise for the systems using $\phi_n(x) = e^{-x} L_n(x)$ and weighting functions $\psi_n(x) = e^{-}$ and $e^{-3x} x^n$ upto a matrix order of 11. Fortunately it was found that eleven functions were enough for convergence to the final solution. The higher order matrices were found to have very small values for their determinants and indicate ill-conditioned matrices. As a result, even after double preci computation, the inverse was likely in error and probably caused instability of the differential equation system (4.67 for large step sizes.

e) Computation Time:

The total time used for the problem was about 20 hours on the IBM 7044 computer. Most of the time was taken up in attempting to calculate accurately the double and single integrals involved in the matrix elements of the final system to be solved. Double integrals evaluated by Gaussian quadrature (See Appendix B) take about 5-10 seconds each to compute as compared to 20-30 seconds each when using a Newton-Cotes formula. The single integrals take about half the time required for double integrals.

The integration of the differential equations for a matrix order of 10 required about 5 minutes for getting values of the distribution in step sizes of 0.005 hrs. from 0 hr. to 5 hrs.

The time required to solve the system of algebraic equations in the steady state case is not significant.

4.10 Suggestions for Future Work:

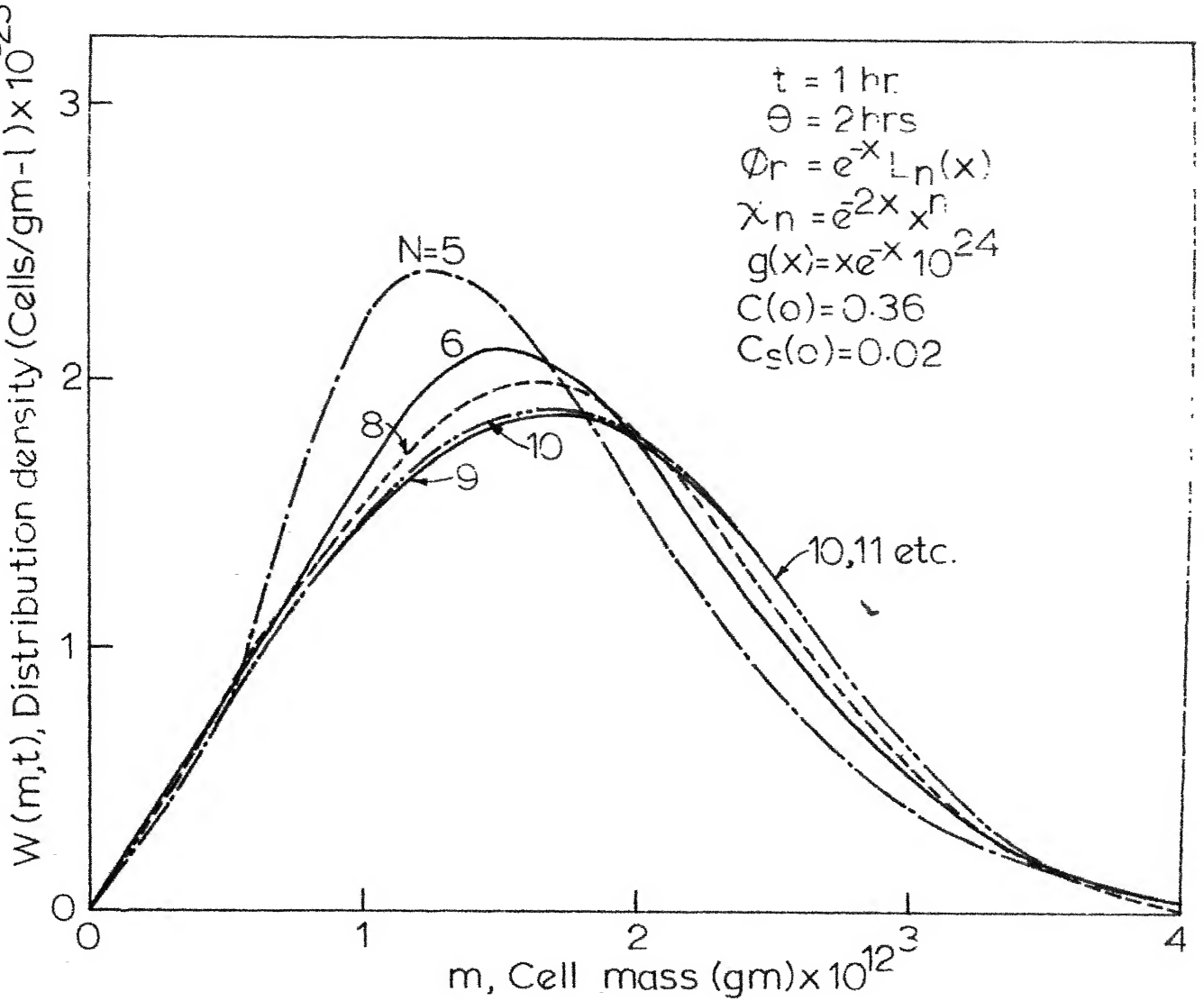
The solutions to the steady state equations were checked quite easily by the method of successive approximations. The method of successive approximation could be applied for the unsteady state equation using the zeroth approximation from MWR. A partial differential equation would have to be solved at each stage by the method of characteristics.

The problem could be solved for the case of spherical cells also which are commonly encountered.

The method of weighted residuals could be extended to solve the system of vector differential equations describing the population balances for a structured, distributed model of a biological culture which is more general in its approach

Partial integro-differential equations of the type solved in this work arise in many other situations involving number balances. MWR could be tried on non-linear equations such as those encountered in a dispersed phase system where coalescence phenomena are considered.

....



Transient solution for a continuous propagator, convergence of solution for fixed time.

Fig 4.8

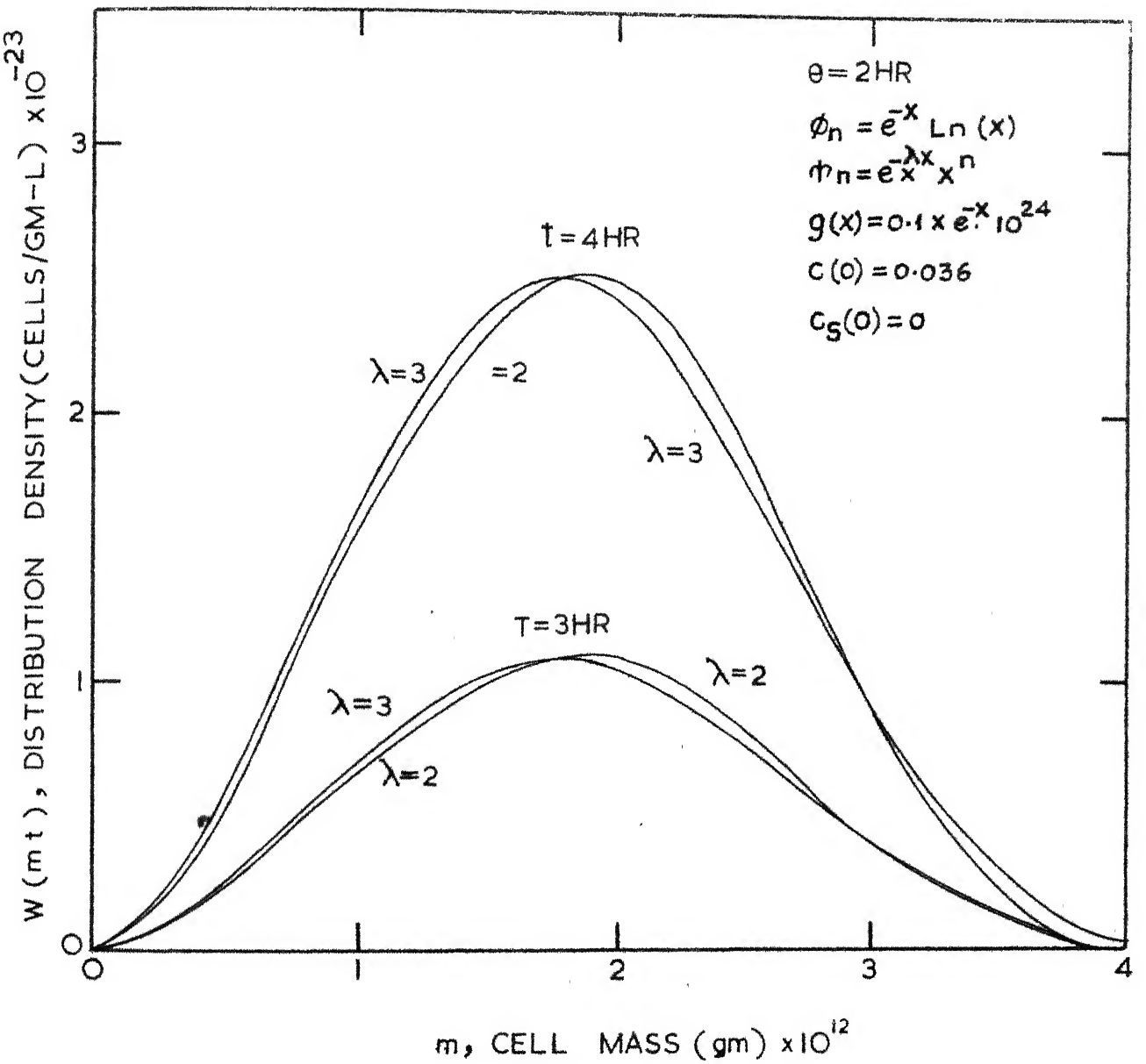
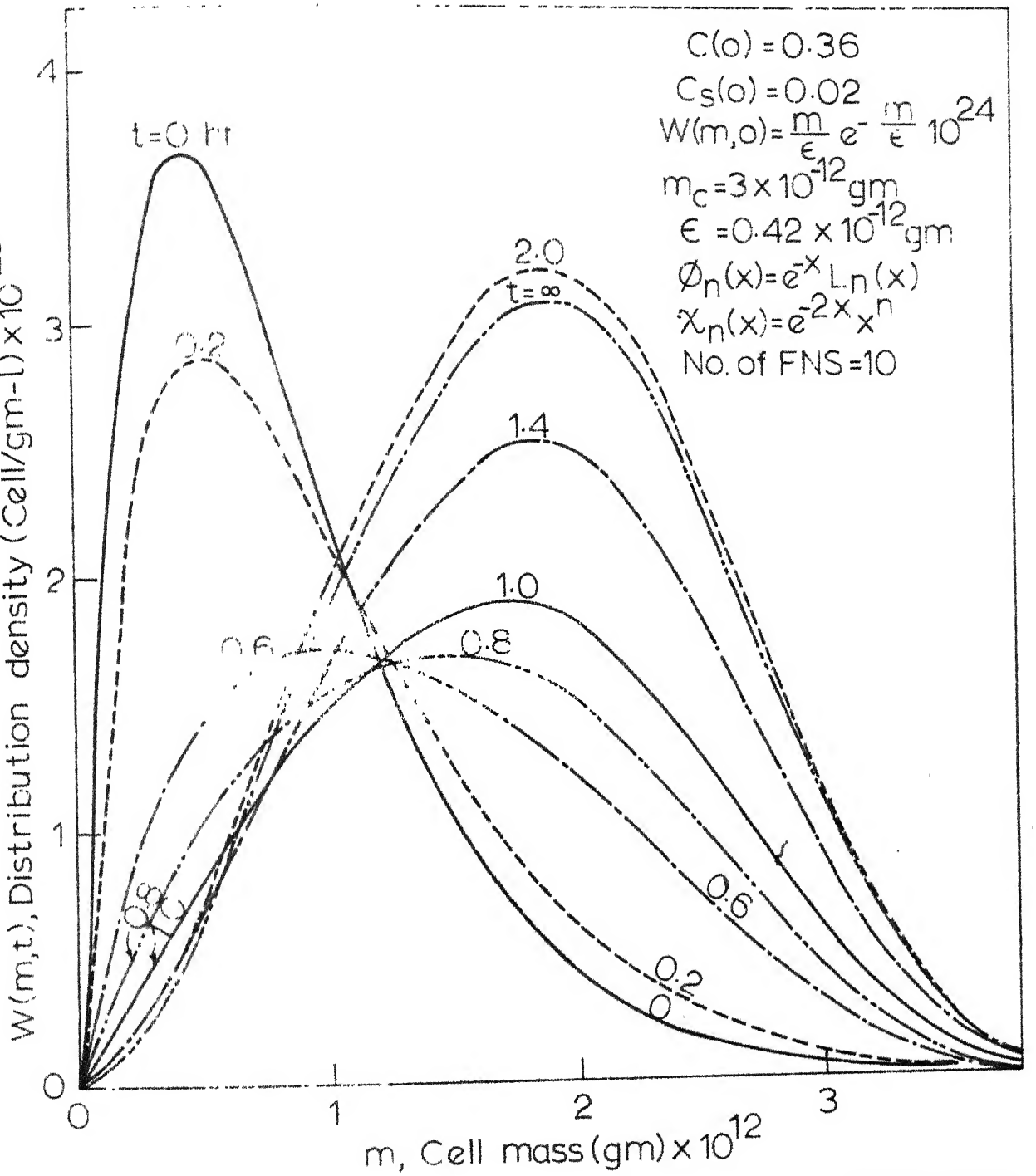
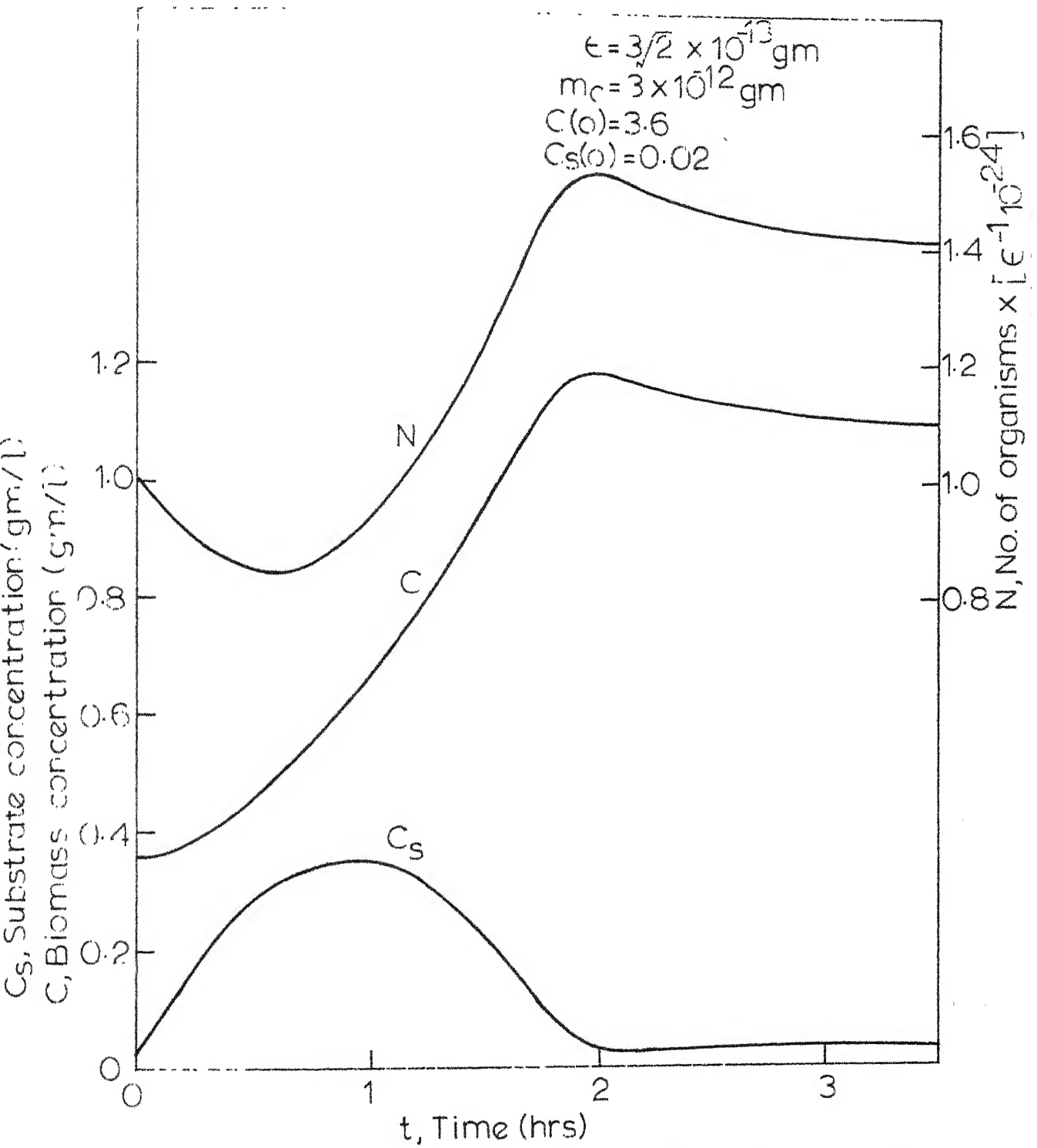


FIG. 4.9 TRANSIENT SOLUTION CONTINUOUS PROPAGATOR COMPARISON OF WEIGHTING FUNCTIONS.



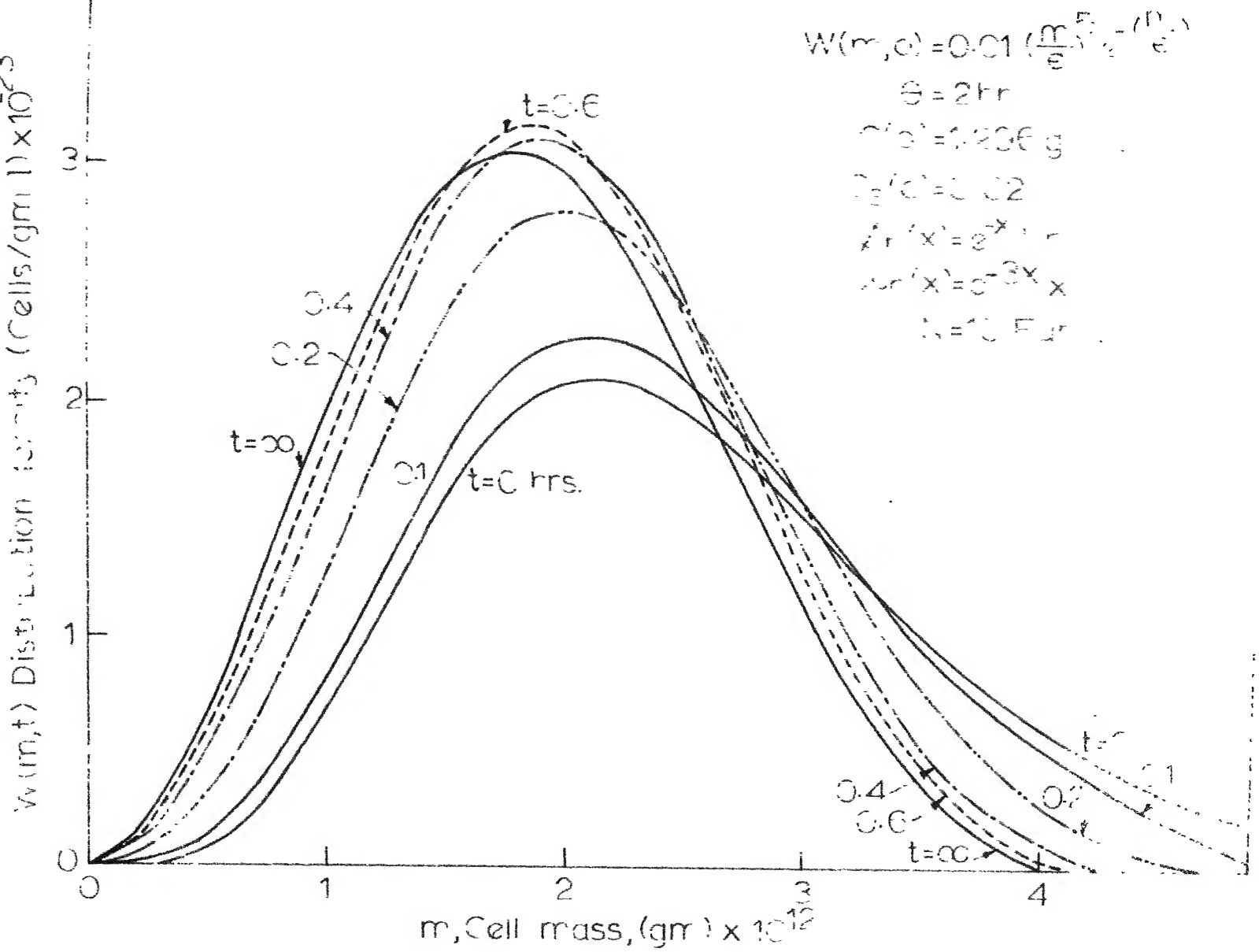
Transient continuous propagator cell mass distribution for initial condition I.

Fig. 4.10

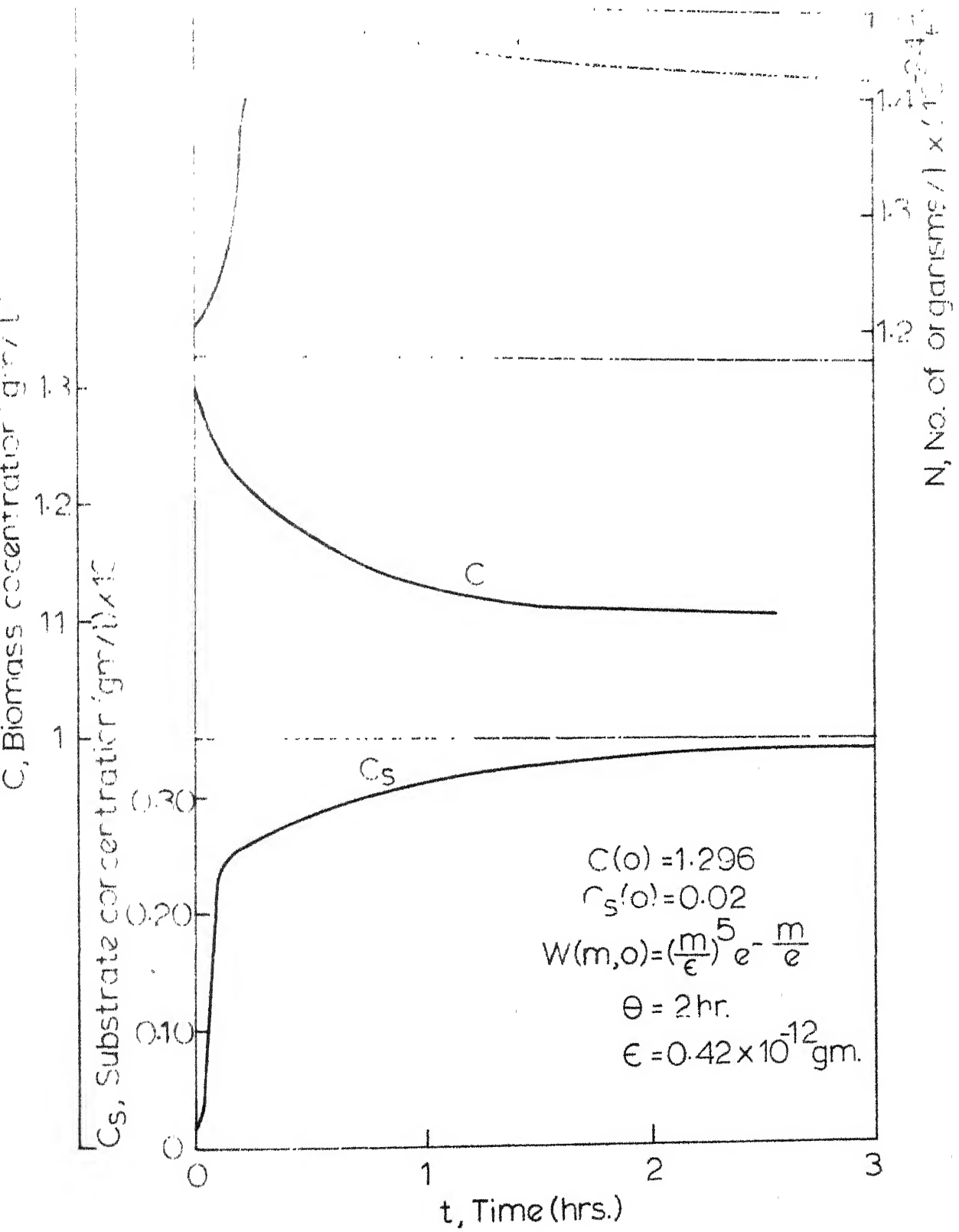


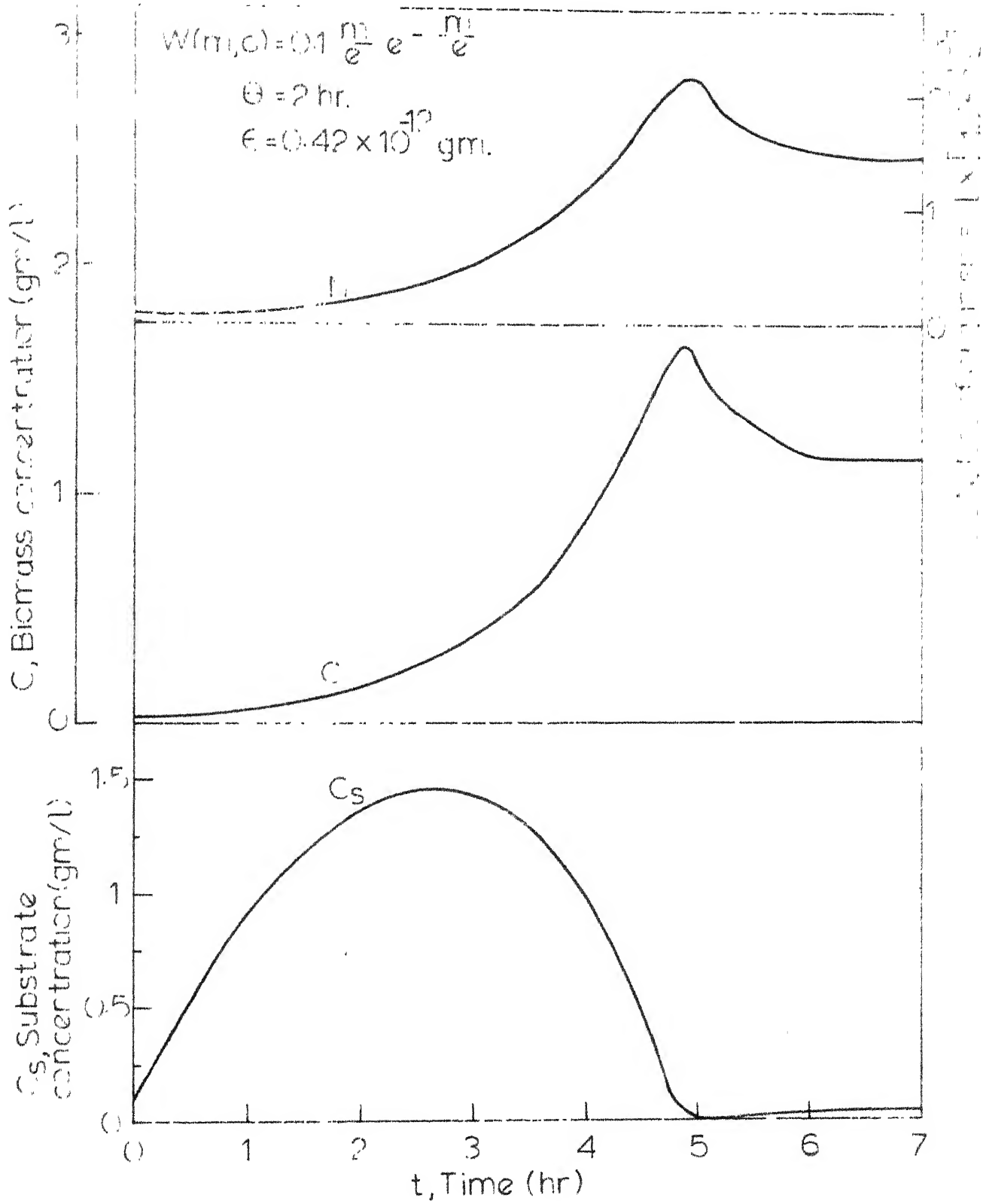
Transient continuous propagator variation of C, C_s, N for

$W(m,o) = \frac{m}{\epsilon} e^{-\frac{m}{\epsilon} 10^{24}}$.

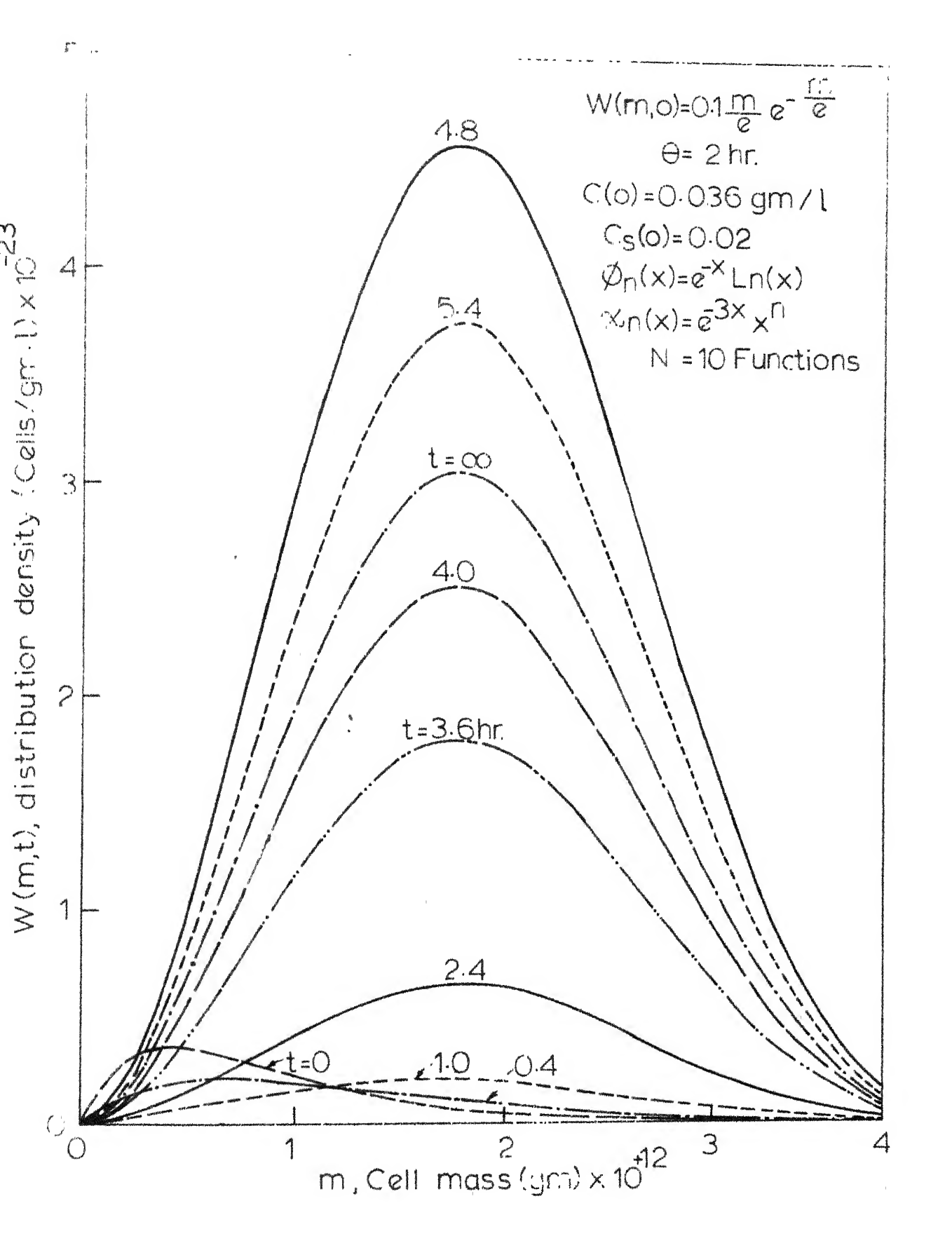


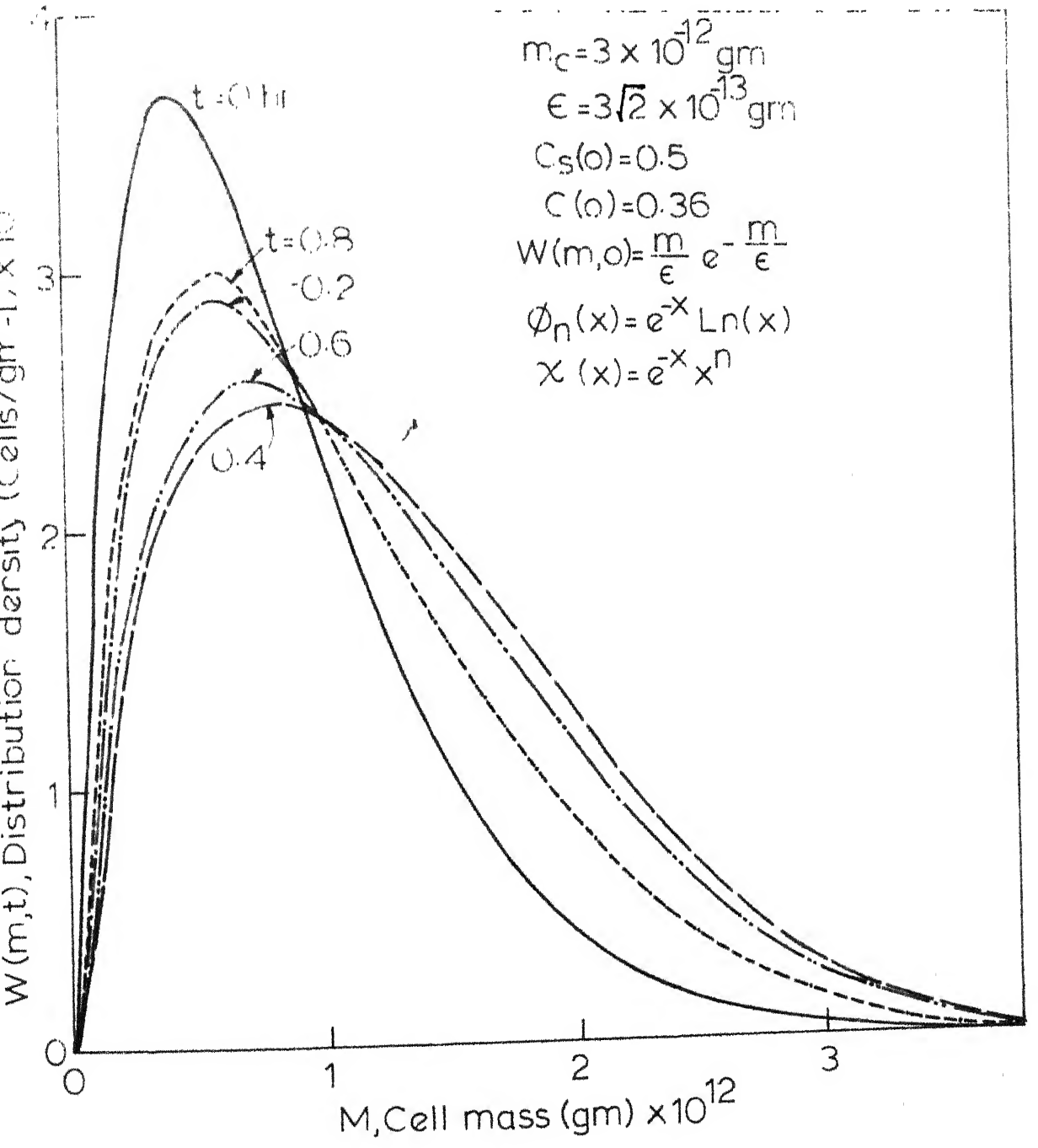
Transient continuous propagator mass distribution for initial condition II.


C, Biomass concentration gm/l
Cs, Substrate concentration gm/l x 10
N, No. of organisms / l x 10
C
Cs
C(0) =1.296
Cs(0)=0.02
W(m,0)=(m/ε)^5 e^- m/e
Θ = 2 hr.
ε =0.42 x 10^-12 gm.
t, Time (hrs.)



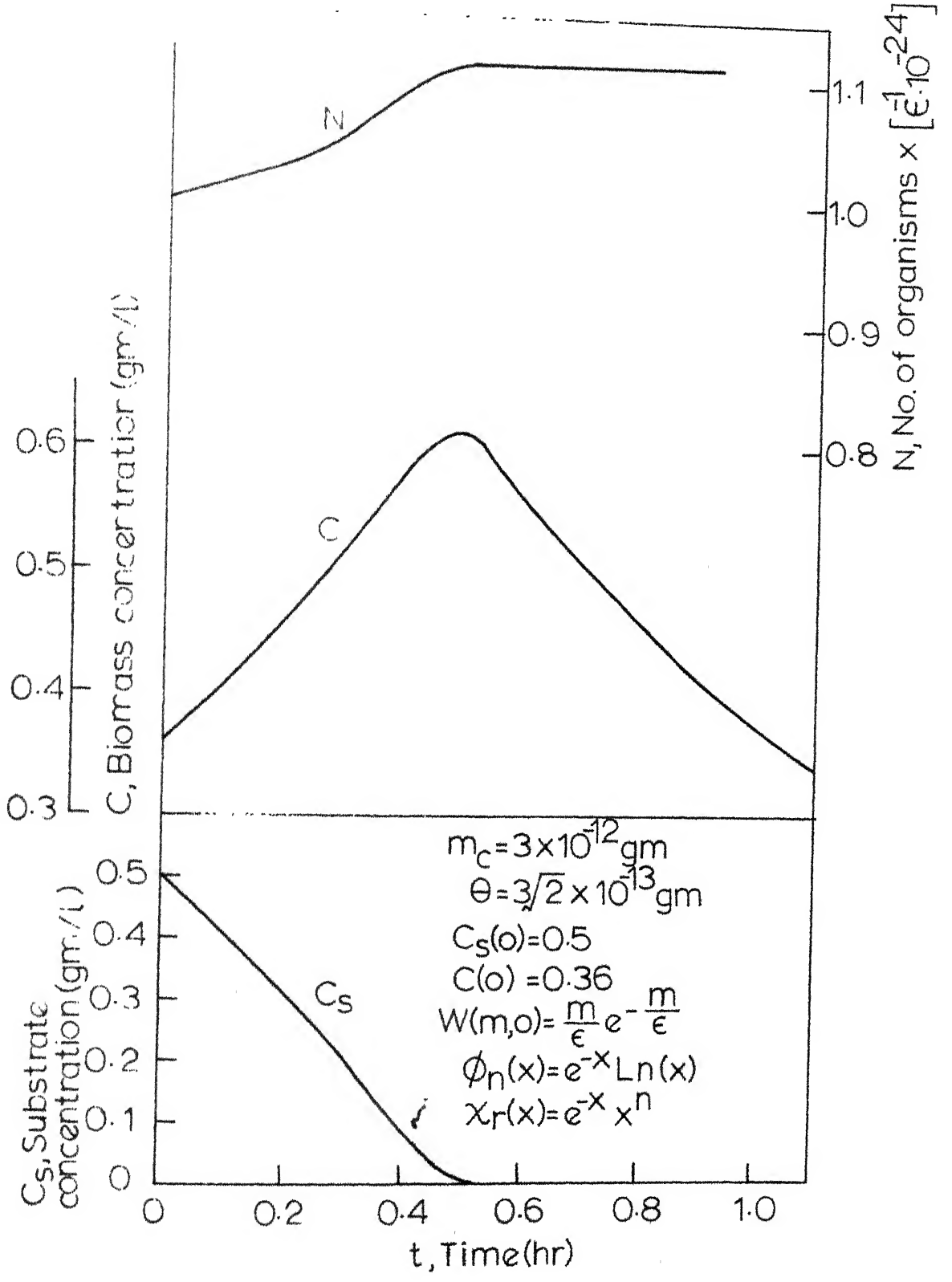
Transient continuous propagator initial condition III.


W(m,o)=0.1 m/e e^-m/e
Θ= 2 hr.
C(o)=0.036 gm/l
Cs(o)=0.02
Øn(x)=e^-x Ln(x)
Xn(x)=e^-3x x^n
N = 10 Functions
4.8
5.4
t = ∞
4.0
t=3.6hr.
2.4
t=0
1.0
0.4
W(m,t), distribution density (Cells/gm.l) x 10^-23
m, Cell mass (gm) x 10^+12
0
1
2
3
4

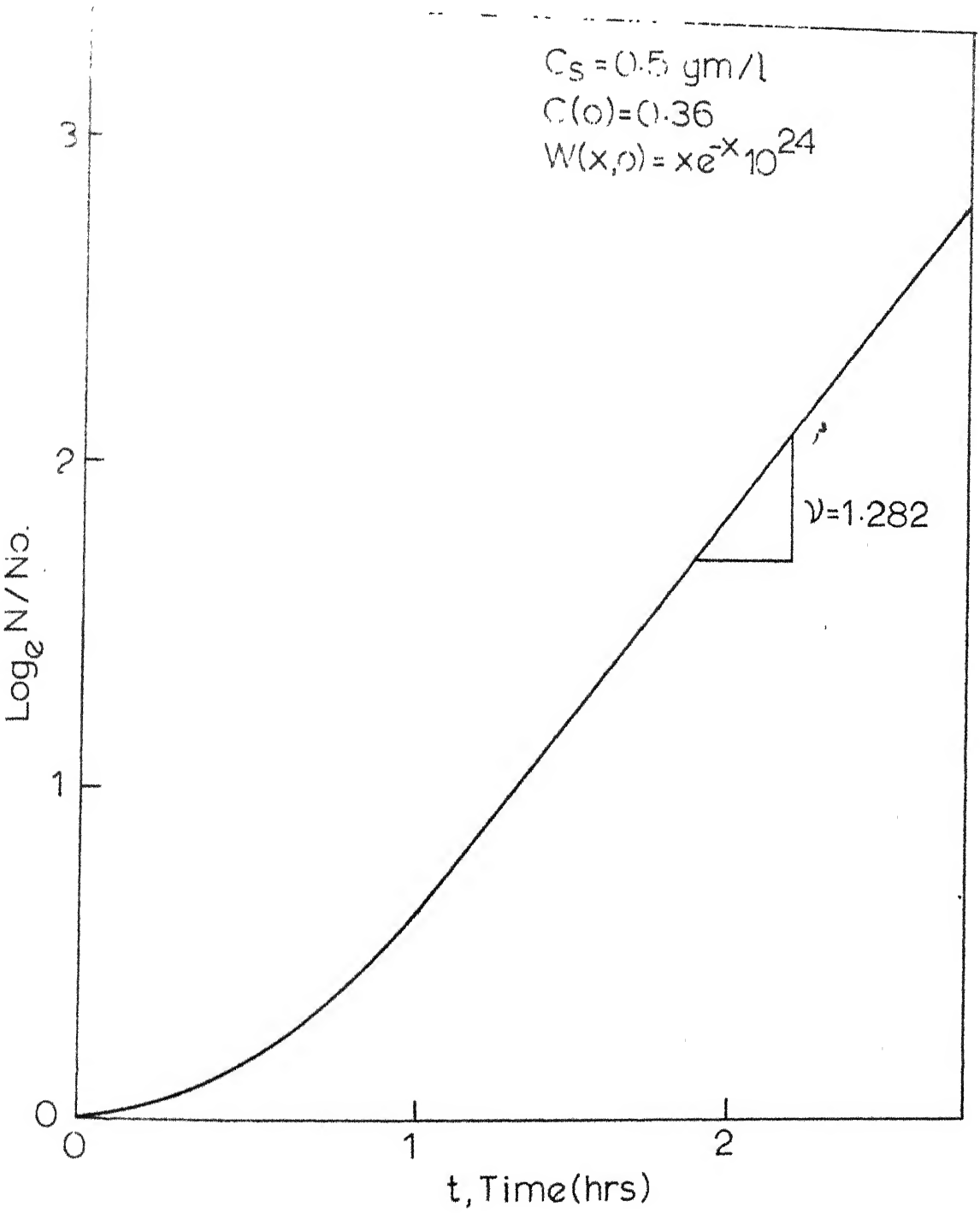


Batch propagator with changing environment.

Fig. 4.16

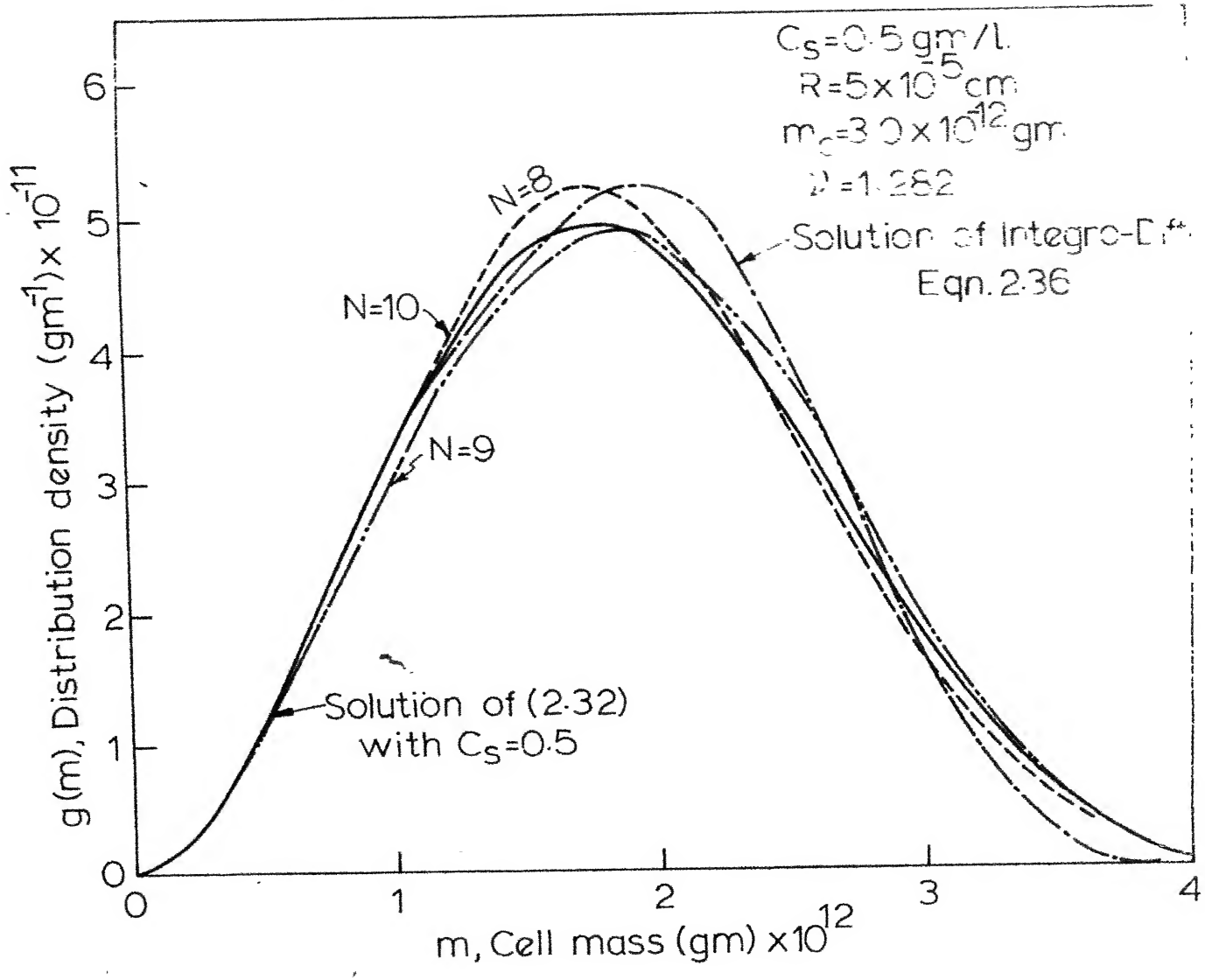


Batch propagator with changing environment.



Asymptotic batch growth curve.

Fig 4.18



Asymptotic batch solution for rod-shaped cells.

Fig. 4.19

APPENDIX - A

LAGUERRE POLYNOMIALS

An important class of orthogonal polynomials which are complete in the space (o, ∞) are the Laguerre polynomials, (27, 28, 31), defined by the formula

$$L_n(x, \alpha, \beta) = e^{\alpha x} x^{1-\beta} \frac{d^n}{dx^n} (e^{-\alpha x} x^{n+\beta-1})$$

$$\alpha > o \qquad \beta > o \qquad n = o, 1, 2 \qquad ..(A.1)$$

For $\alpha = \beta = 1$ one has the ordinary Laguerre polynomials.

$$L_n(x) = e^x \frac{d^n}{dx^n} (e^{-x} x^n)$$

$$= \sum_{\nu=o}^{n} \binom{n}{\nu} \frac{n!}{\nu!} (-x)^{\nu} \qquad \ldots \qquad \ldots(A.2)$$

For the general case

$$L_n(x, \alpha, \beta) = \sum_{\nu=o}^{n} \binom{n}{\nu} (\beta+\nu; 1; n-\nu) (-\alpha x)^{\nu} \ldots(A.3)$$

where

$$(m:d:\nu) = m(m+d)(m+2d) \ldots\ldots m+(\nu-1)d$$

$$\nu = 1, 2, \ldots\ldots$$

$$(m:d:o) = 1$$

The first few Laguerre polynomials are thus

$$L_o(x, \alpha, \beta) = 1$$

$$L_1(x, \alpha, \beta) = \beta - \alpha x$$

$$L_2(x, \alpha, \beta) = \beta(\beta+1) - 2(\beta+1)\alpha x + \alpha^2 x^2 \quad \ldots(A.4)$$

The Laguerre polynomial $L_n(x, \alpha, \beta)$ has n distinct real roots in (o, ∞) and any function multiplied by $L_n(x, \alpha, \beta)$ will show oscillatory behaviour.

The family (A.3) satisfies the orthogonality condition

$$\int_0^\infty e^{-\alpha x} x^{\beta-1} L_n(x,\alpha,\beta) L_m(x,\alpha,\beta)\, dx$$

$$= 0 \qquad m \neq n$$

$$= \frac{n!\,\Gamma(\beta+n)}{\alpha^\beta} \qquad m = n \qquad \ldots(A.5)$$

To normalise the polynomials (A.3) they should be divided by

$$\frac{n!\,\Gamma(\beta+n)}{\alpha^\beta}$$

Laguerre polynomials satisfy the recurrence relation

$$L_{n+2}(x,\alpha,\beta) + (\alpha x - 2n - \beta - 2) L_{n+1}(x,\alpha,\beta) + (n+1)(n+\beta) L_n(x,\alpha,\beta) = 0$$

$$n = o, 1, 2 \qquad \ldots \qquad \ldots(A.6)$$

and the Laguerre differential equation

$$x L_n''(x,\alpha,\beta) + (\beta - \alpha x) L_n'(x,\alpha,\beta) + n\alpha L_n(x,\alpha,\beta) = 0$$

$$n = 0, 1, 2 \qquad \ldots \qquad \ldots(A.7)$$

It may be shown using the orthogonality property that

$$\int_0^\infty e^{-\alpha x} x^{m+\beta-1} L_n(x,\alpha,\beta)\, dx$$

Expansion of Functions in Series of Laguerre Polynomials (28)

One of the most important properties of the Laguerre polynomials is the fact that a real function $f(x)$ defined in the infinite interval (o, ∞) can be expanded in a series of the form

$$f(x) = \sum_{n=o}^{\infty} C_n L_n (x, \alpha, \beta) \qquad 0 < x < \infty \qquad \ldots(A.9)$$

provided $f(x)$ satisfies certain conditions. The coefficients C_n can be determined using the orthogonality property (A.5). The expansion (A.9) is valid if $f(x)$ is piecewise smooth in every finite interval $[x_1, x_2]$ and suitably well behaved near the points $x = o$ and $x = \infty$.

APPENDIX - B

GAUSSIAN QUADRATURE USING LAGUERRE POLYNOMIALS (30)

For the evaluation of integrals over infinite intervals, there are two approaches (1) Use a knowledge of the integrand to bound the magnitude of the integral from some finite value to infinity by a positive constant $\epsilon > 0$ and then use a quadrature formula for the remaining finite- interval. (2) Use a quadrature formula especially developed for the infinite interval. The latter approach is more convenient and is economical in terms of computer time. The former can be used as a check when necessary.

The Laguerre-Gauss quadrature formula is given by (30)

$$\int_0^\infty e^{-x} f(x)dx = \sum_{j=1}^{n} H_j f(a_j) + E \qquad \ldots(B.1)$$

Where the a_j's are the zeroes of $L_n(k)$, the Laguerre polynomial of nth order. (See Appendix A) the H_j's being given

$$J\ H_j = \frac{(n!)^2}{L_n'(a_j)\ L_{n+1}(a_j)} \qquad \ldots(b.2)$$

The error term E is

$$E = \frac{(n!)^2\ f^{(2n)}(\eta)}{(2n)!} \qquad \ldots(B.3)$$

η lies in (o, ∞)

If f(x) is continuous, any desired degree of accuracy is

obtainable by using a sufficiently high order formula, by increasing n, the number of quadrature points in (B.1). Using a sequence of Gaussian formulae like (B.1) with increasing n will lead to a convergent sequence of approximations. The x_j's and w_j's in (B.1) have been listed for n=2 to 32 in the appendix of (29).

APPENDIX - C

DATA FOR ROD-SHAPED CELLS (7)

m_c, mean division mass = 3×10^{-12} gm

ϵ, measure of spread in division mass distribution = $3\sqrt{2} \times 10^{-13}$ gm.

ϕ_m, maximum flux across cell surface, used in the growth rate of a single cell = 6×10^{-5} gm/cm^2-hr.

K_s, Michaelis - Menten constant in the flux term of growth rate expression = 0.02 gm/liter

μ_c, proportionality constant for rate of release of mass by cell = 1 hr^{-1}

β', fraction of substrate in mass taken into the cell = 0.75

C_s^o, substrate concentration in entering stream = 2.5 gm/cm^3

ρ, mass density of cell = 1.01 gm/cm^3.

NOMENCLATURE

C	Biomass concentration, grams/litre
C_i	Coefficient of ith approximating function in trial solution
C_{sk}	Concentration of kth substrate (C_s if single limiting substrate), grams/litre.
C°_{sk}	Concentration of kth substrate in feed stream, grams/litre
$f(t)$	Function of time in cell growth rate expression
$g^*(m)$	Density of cell mass distribution in a symptotic growth gram^{-1}.
$g(m)$	Initial cell mass distribution cells/litre-gram
$h'(m)$	Density of division mass distribution gram^{-1}
K_s	Michaelis-Menten kinetics saturation constant, gram/litre
L_n	nth Laguerre polynomial
l	Length of rod-like cell, cm.
m,m'	Cell mass, gram
m_c	Mean division mass of a cell, gram
N	Population density, cells/litre Number of Approximating functions in trial solution.
$p(m,m')$	Density of daughter cell mass distribution, gram^{-1}.
R	Radius of cell (rod), cm.
$R(m)$	Residual of the differential equation
$r(m,C_{sk})$	Cell growth rate grams/hr. in environment C_{sk}
r'	Rate of cellular mass uptake grams/hr.
r''	Rate of cellular mass release, grams/hr.
S	Surface area of a cell, cm^2
t	Time, hr.

$W(m,t)$ Number density of cells, cells/gm-litre.

$w(x,t)$ Transformed number density cells/gm-litre

x,y Variables used for mathematical manipulations, defined where used in text.

GREEK LETTERS

β_i' Fraction of ith component in mass taken into cell (β if a single limiting substrate)

λ Specific probability of fission hr^{-1}

ν_i' Fraction of component i in mass released by cell.

δ Dirac delta function

ϵ Measure of spread in division mass distribution, gram

$H'(m, C_{sk})$ Specific death probability hr^{-1}

θ Holding time, hr.

λ Constant in weighting function expression

μ Specific rate of biomass increase hr^{-1}.

μ_i ith moment of the distribution density

μ_c Specific mass release rate hr^{-1}.

ν Specific rate of population increase

ρ Mass density of cell $gram/cm^3$

τ Cell age, hr.

ϕ Mass flux across cell surface $gram/cm^2$-hr.

ϕ_m Maximum mass flux across cell surface $gram/cm^2$-hr.

ϕ_n nth approximating function in trial solution

ψ_n nth weighting function

$\sim$ Over a quantity means it is evaluated in the steady

$-$ Over a quantity means it is a vector

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